Goitre with special Reference to its Occurrence in School Children.

THESIS

for the M.D. Glasgow

submitted by

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Distribution of Goitre throughout the World.

Simple Parenchymatous Goitre in a girl

13 years of age.

Simple Parenchymatous Goitre in four school girls
age 12 - 14 years.
Under treatment with thyroid treatment.

Simple parenchymatous goitre of moderate size.

GOITRE, WITH SPECIAL REFERENCE TO ITS OCCURRENCE IN SCHOOL-CHILDREN.

SECTION I.

My special interest in this subject dates back to the time when first I came to practise in the North of England. Previous to that time I had lived in Lanarkshire, Ayrshire, and other parts of Scotland, and although I had met with cases of exophthalmic goitre, cretinism, and myxoedema, I had not observed many cases of simple goitre. When I came to the Newcastle area I found enlargement of the thyroid much more prevalent than in any of the districts of Scotland where I had previously worked. Coming to Yorkshire some years later I saw many cases of goitre both among school children and adults. Cretinism associated not only with the usual physical dwarfism and mental retardation but with enlargement of the thyroid gland was also encountered. As a matter of fact it was whilst making an investigation into the prevalence of mental deficiency in the Halifax area of the West Riding of Yorkshire that I came into contact with these cretins. When transferred

to Manchester some years ago I began to make more systematic investigations into the occurrence of goitre and I have come to the conclusion that goitre is more prevalent here than in any of the districts where I had previously lived. It has appeared to me that the further south I have come the greater has been the incidence of goitre. There is undoubtedly a much higher incidence of goitre in Manchester than in Glasgow. There are also more cases of goitre to be seen on the west side of the Pennine Chain than on the east. In fact there is apparently a gradual increase in the prevalence of goitre along the Pennine Chain from north to south, reaching a maximum in the valleys of Derbyshire and Lancashire.

Endemic goitre may be defined as a chronic enlargement of the thyroid gland, not due to neoplasm, occurring endemically in certain localities. Generally it is associated with mountainous regions although not invariably so, and it is usually limited to temperate and subtropical zones.

Goitre is a generic term including several different conditions. Classification has always presented difficulty. There is in the literature a diversity of nomenclature.

Hertzler, (Hertzler, A.E. Diseases of the Thyroid Gland, Endocrinology t. vi. p.6. 1922) made a classification based on his pathological findings. To Dr. H. Plummer belongs the credit of classifying goitres on a reasonable basis. He made observation of the cases passing through his hands and later compared his findings with the pathological condition of those glands that were removed by operation. His results were published in the American Journal of Medical Science in 1913. pp.790-796. He divides goitres into three types (1) simple colloid goitre. (2) Graves' disease or hyperplastic goitre, and (3) toxic adenoma. Since 1913 very little substantial difference from Plummer's classification has been made. In Price's "System of Medicine" 1926, goitres are divided into three groups - (1) exophthalmic goitre (2) goitre - simple etc. and (3) Tumours. It is true, as W.M. Boothby points out (Endocrinology Jan. 1921. Vol.5) that in Plummer's classification two separate and distinct types of hyperthyroidism have to be recognised, but these are clearly differentiated, the one being associated with the clinical syndrome of true exophthalmic goitre and accompanied by diffuse

hypertrophy and hyperplasia of the thyroid gland, the other not being accompanied by this diffuse hyperplasia but with the occurrence of adenoma in the gland. As recently as August 1926 Allen Graham (Journal of the American Medical Association Aug.28th, p. 628) criticises Plummer's division stating that there is no sign nor symptom pathognomonic of exophthalmic goitre - as opposed to toxic adenoma - nor any histological alteration in the gland of positive definite distinction. He believes that toxic adenoma and exophthalmic goitre are variations of one and the same morbid state. Although it is true, as Sir James Berry states, that a simple goitre may become "Basedowified", still there does not seem sufficient reason for departing from the classification already given by Plummer.

Simple goitre is the goitre of adolescence and is characterised by hypertrophy without hyperplasia. There is a great increase in colloid production. Symptoms may be entirely absent. Swelling of the thyroid gland is frequently first noticed about puberty and this has led some to consider simple goitre as secondary to the commencement of

Age 5.

Goitre noticed by parents when child two years old, but not brought for treatment till age 5.

The social conditions are very bad in this case.

menstrual life in the female. Many of these thyroid enlargements that appear about the age of thirteen in girls and a year or two later in boys are small and temporary, disappearing without treatment in a few years. Temporary swellings of this nature may be looked upon as a physiological increase to meet an increased demand. On the other hand thyroid enlargement may occur long before puberty. When children are brought to me suffering from goitre the parents sometimes report that the thyroid swelling has been present since birth. Recently a girl five years of age was presented for treatment. (See photograph). Projecting forwards from the thyroid isthmus there was a swelling about the size of a pigeon's egg but being covered with the skin and other tissues it appeared larger. The child's father informed me that this condition had been present for at least two years. The swelling was in the middle of the neck, was soft to the touch, and moved up and down with deglutition. It was not tender and apparently caused the child no discomfort and no concern.

The thyroid swelling is usually symmetrical. Where one lobe is enlarged more than the other it is usually the right lobe that is the larger. Lately I examined an enlarged thyroid in a girl fifteen years of age and found that the swelling was entirely an enlargement of the left lobe. My experience leads me to believe that such left-sided goitres are unusual.

Thyroid enlargements are often soft to the touch especially in young subjects. Sometimes they feel firmer to the touch and may be irregularly knotted with small cysts. Sometimes one or two large fluctuating masses can be felt on palpation. "Parenchymatous" is a term applied loosely to a general swelling of the whole gland as distinguished from local enlargement due to adenomata. Goitres vary in size in children and in adults. In adults they may be as small as walnuts or as large as melons. Foedére, according to Robinson, speaks of one eight pounds in weight, and Abelard describes a goitre reaching to the thigh.

Alibert (Nosologie Naturelle I. p.466. Plates C and D.) figures a goitre reaching to the waist. Some have described goitres reaching from ear to ear closing up the external auditory meati, causing deafness. Such large goitres fortunately are very unusual. In children the average size is less than a golf ball but the swelling may be bigger than a tennis ball or as small as a hazel nut. Frequently there is an entire absence of symptoms. Apart from the annoyance of a rather disfiguring swelling in the neck the school-girl may make no complaint. On enquiry being made a history of rheumatism is often obtained. Hirsute deficiency is often present and constipation is a frequent accompanying factor. In fact Bainbridge (International Journal of Medicine and Surgery, Jan. 1926) considers that the thyroid enlargement is often caused by systemic poisoning due to intestinal toxaemia. The voice is sometimes poor in quality. Difficulty in swallowing is occasionally complained of. Breathlessness is quite unusual in children but cyanosis has been observed in a few cases.

As defined above this disease excludes cancer. Thyroiditis due to septic infection is not included and the same applies to the Thyroiditis of Chagas which is endemic in Brazil and is due to a trypanosome finding entrance into the human subject through the bite of an insect. This latter disease is associated with pain and swelling of the thyroid gland, and causes an enormous mortality amongst infants in South America.

Owing to the prevalence of endemic goitre in Derbyshire this condition is frequently spoken of as "Derbyshire neck" in the northern counties of England. Being common along the Nith valley in the South of Scotland it is often spoken of there as "Nithsdale neck". The early Greek writers referred to it as Bronchocele(Gr. βρογχος) but the term in common use now is that of simple or endemic goitre, a name first applied by the French and Swiss writers most probably from its connection with the throat (Lat. guttur = the throat).

In this present thesis I propose to give an account of goitre as I find it in young people. There is a peculiar

distribution of goitre here which bears a relationship to the geographical and geological features of the district. I hope to give a detailed account of this. Nationality, in my opinion, is a factor too of some importance. I intend to give an account of my experience in the treatment of goitre among school-children and the conclusions I have come to as a result of the past two years' work.

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SECTION 2.

Historical Outline.

The chronicle of goitre dates back to very early times. The first allusion to this subject is to be found in the Atharva Veda, an ancient collection of Hindu exorcisms to be employed on behalf of those suffering from this malady.

In the "golden age" Hippocrates, sometimes styled "the Great", said with reference to the choice of drinking water, (Hippocrates and His Successors, by R. Moore, pp.21,22) "The man who is strong and well need not be particular but can drink the water which is nearest to him". Experience seems to have led him to modify his views, for we find that in later life he attributed to the water coming from snow and ice great influence in the production of certain diseases, especially goitre.

The period immediately following the days of Hippocrates is very barren of medical literature. In connection with the "Alexandrian School" the names of Herophilus and Erasistratus are noteworthy. The latter wrote extensive

treatises and attributed excessive eating and drinking as the causes of many of the diseases that human flesh is heir to. He introduced venesection, fasting and bandaging. It is an interesting fact that even to-day one often sees cases of goitre where a bright velvet neck band has been applied around the neck with a view to reducing the swelling. Even the Abyssinians tattoo a string of beads around the neck for the same purpose.

When Rome became mistress of the world Greek physicians found their way to Rome. Every fibre of the Roman being became permeated with Hellenism as Max Neuburger says (History of Medicine p.213). The writings both of Cicero and Seneca reveal this fact. A writer of this period, Vitruvius by name, makes mention of the aqueducts of that time and dwells on the disadvantages of leaden pipes. He also remarks that goitre was prevalent among the farmers of Italy and the Alpine dwellers. In his "Satires" Juvenal also refers to the occurrence of goitre in the Alps - "Quis tumidum guttur miratur in Alpibus" (Juv.13.162.) Pliny also writes "guttur homini tantum ut suibus intumescit".

(Pliny 11. 17,68.) (Outlines of Greek and Roman Medicine by J. Elliott pp. 84-85).

Cornelius Celsus, a Roman patrician who lived during the first century, gives the most complete account of medical science in Roman times (De Re Medica). Robinson in his thesis "Goitre or Thyrocele" refers to the advice of Celsus in cases of goitre, namely, the application of caustic for its removal.

The period of Arabian medicine begins with the burning of the Alexandrian library by the followers of Mahomet A.D. 640, and ends with the fourteenth century. (Medical and Surgical Science by J. Hillier, p.27.) In the eleventh century the Arabian Albucasis was a prominent writer. He wrote a treatise which was the leading text-book on surgery during the middle ages (Garrison, History of Medicine,p.89) He likens the swelling due to goitre to the dewlap of the turkey.

In the 13th century Marco Polo, the famous Venetian voyager, writes in chapter 35 of his remarkable account of his travels "Yarcour is a province five days' journey in

extent..... the inhabitants are great craftsmen, but a large proportion of them have swollen legs and great crops at the throat which arise from some quality in their drinking water". (Colonel Yule's translation). In the fifteenth century a prominent figure comes before us in the person of Paracelsus. Osler (Evolution of Modern Medicine p. 135) describes him as the Luther of Medicine, the very incarnation of revolt. He ignored the conclusions of all his predecessors and set himself out to be "the most glorious man on earth". Robert Browning in his "Paracelsus" puts these words into the mouth of this great man,

> "The lore you praise and I ignore,
> The labours and the precepts of old time,
> I have not lightly disesteemed, but, friends,
> Truth is within ourselves."

Paracelsus gives an excellent description of goitre in the region of Salzburg where he was born. He was the first, moreover, to establish a correlation between goitre and Cretinism (Opera Omnia Strasburg 1603 pt.ii pp.174-182).

In the sixteenth and seventeenth centuries - the age, moreover, in which Harvey, Sydenham, Kepler, Galileo, and

Newton lived – there is no writing of great importance in connection with goitre although Hirsch gives a list of authors who wrote at this time on the prevalence of goitre in the Alps, the Pyrenees, the Atlas mountains, and elsewhere.

Thomas Gage, in his "New Survey of the West Indies 1648",speaks of his journey from the city of Chiapa to Guatemala and describes his visit to a place called Sacapula, "I found," he says, "in a harbour by the water side the Prior of Sacapula..... at the first sight I was a little daunted to behold the Prior who looked most fearfully with a bladder from the throat swelled almost round the necke which hung over his shoulders and breast, and stayed up his chin, and lifted up his head so that he could scarce look anywhither but up to heaven. In our discourse he told me that this disease had been upon him at least ten years, and that the water of the river had caused it in him and in many others in that town."

In the eighteenth century medicine as a profession reached its zenith, associated as it is with the names of Hunter, Laennee, and Jenner. Morgagni, who lived from 1682 till 1771 greatly extended our knowledge of post-mortem appearances. He suggested that the function of the thyroid gland was to secrete a glairy colloidal substance, an observation which has been amply sustantiated in more recent times. Boerhaave also lived at this time. He is probably the greatest teacher of clinical medicine recorded in history. At a time when most varied ideas were held about the function of the thyroid gland Boerhaave maintained that it had mainly to do with the improving of the voice. (He may have noticed how often the goitrous had poor toneless voices).

Medical literature up to about A.D. 1800 is rich with references to the use of organic substances for medicinal purposes. According to Biedl there were 152 products of animal origin in the apothecary shops of Innsbruck in 1765 (Biedl, Internal Secretions.....1922). In 1775 Theophile de Borden speculated that each organ of the body was the

laboratory of a specific substance necessary for the proper functioning of the whole organism. Other workers followed, such as Berthold, who in 1849 demonstrated an internal secretion to the gonads. In relation to the thyroid gland Fodére published his essay on the occurrence of goitre and cretinism in the Maurienne and Aosta valley. This was followed in 1800 by his treatise on "Goitre and Cretinism". In 1820 Coindet showed the value of Iodine in the treatment of goitre, and in 1850 Curling first described sporadic cretinism. This same year Anton Wolfler of Kopigeu, Bohemia, (who introduced the operation of gastro-enterostomy) devoted special attention to the surgical treatment of goitre.

About this time the Sardinian government appointed a commission to investigate the causes of endemic goitre and to suggest a remedy. This was followed by a French commission in 1864. More recently the Swiss also have made an investigation into goitre and cretinism. Masters in his "Conquest of Medicine" says that although doubtless countless sufferers from goitre would give almost anything to see the

swelling in their necks disappear, yet in some parts of the continent of Europe the people have actually regarded goitre as a blessing. Mothers expressed delight when they noticed the necks of their male children beginning to show signs of swelling. The reason for their satisfaction was due to the fact that goitre would ensure exemption from military service. Saint Leger,on page 351 in his book "Etudes sur les Causes du Cretinisme et du Goitre Endemique" gives the number of cretins and goitrous in the districts of Piedmont and Savoy and gives a total of 7084 cretins (= 0.27%) and 21841 goitrous. Some of the valleys of France and Switzerland were full of goitre and the report of the Sardinian commission in 1848 contained startling figures of which those given above are examples. Wherever goitre existed cretinism abounded. On every hand were to be met stunted cretins in a state of imbecility. Especially in the Vale of Aosta and the canton of Valais were these cretin communities to be found till finally the Swiss Government stepped in and segregated the sufferers. The French Government likewise made valiant

efforts to cope with the disease by giving minute doses of Iodine to school-children. The results were excellent but unfortunately the parents undid much of the benefit achieved by giving the most goitrigenous waters available to their male children to prevent their recovery. In Savoy and the French Alps nine out of every hundred men had to be excused military service on account of goitre.

In 1835 Graves of Dublin published an admirable description of exophthalmic goitre (Graves, London, Med. and Surg. Journ. 1835 pt 2 p.516). In 1840 Basedow gave an account of the " Mers Triad". Previous to that date Parry, a Bath physician, had given a full description of this disease which was published after his death in 1825. The Italians claim that Flajani was the first to describe this disease. He wrote in 1800 but Moebius tells us that Flajani's account is meagre and inaccurate and bears no comparison to the later most excellent account given by Parry. A fresh impulse was given to the doctrine of internal secretion by Claude Bernard's work on the glycogenic function and Addison's account of suprarenal disease in 1849 (Garrison

History of Med. p.603). In 1856 Moritz Schiffz, a German physiologist, excised the thyroid gland of a dog. The animal died with cachectic symptoms. He carefully examined the vago-sympathetic nerves to make sure that death was not due to nerve injury. He concluded that the thyroid gland was an organ important to the functioning of the body. Munk on the other hand maintained that death in these extirpation experiments was due to nerve injury. The work of these early experimenters led to no very definite conclusions. The importance of the parathyroid glands was overlooked - although Sandstroëm discovered them in 1880 and Gley made an examination of the function in 1891. The work of Paton and Koch revealed the presence of toxic substances such as guanidim and cholin in the blood of parathyroidectomised animals which gave rise to toxic effects. Vassali and Generali observed that a parathyroidectomised animal died in a few days after the appearance of nervous symptoms such as tremor, rigidity of the hind legs, asthenia, incoordination and convulsions. In 1884 Reverdin and Kocher observed that removal of a goitre was followed by symptoms

which Semon recognised as analogous to Myxoedema. Hofmeister and von Eiselsbung by excising the thyroid gland directly after birth were able to produce artificial cretinism (Victor Horsley, B.M.J. 1896, pt. 2, pp. 1623-1625). The characteristic changes in the epiphyses led Eherth to speak of "foetal rickets". In 1891 G.R. Murray introduced the treatment of myxoedema by hypodermic injections of thyroid substance. In 1892 Hector Mackenzie and G.L. Fox demonstrated that oral administration of thyroid gland was as effective as hypodermic injection. Victor Horsby summarises the results obtained up to this time by the experimental workers. He says that thyroidectomy in birds and rodents is followed by no cachexia, a slowly developing cachexia in ruminants, a moderate cachexia in man and in the monkey, but a rapid and severe cachexia in carnivora. He concludes that the thyroid gland plays a definite part in the economy; that it is intimately connected with the metabolism of the blood and the tissues, and that a colloid substance is elaborated

which is transmitted by way of the lymphatics to the circulation. (Horsley, B.M.J. 1892 pt.1. pp. 215-219). Much work has been done in recent years on the histology of the thyroid gland. The epithelium has been specially studied by Langendorff, Hürthle, Neumeister and Anderson. Langendorff observed that there were two types of cells in the walls of the thyroid vesicles, (1) the "chief cells", far more numerous, clear and finely granular and (2) the "colloid cells" which are larger, more granular, and stain more deeply than the first variety. These alveolar cells are of the merocrine type, that is to say that only part of the cell is used in the secreting process. When the colloid cell is full the nuclear membrane ruptures and the secretion is evacuated into the lumen of the alveolus. After this the cell is regenerated and becomes a chief or principal cell ready to start afresh on the secretory cycle. (Crotti p.22). Hürthle describes fine channels joining the alveoli with the lymph spaces. It is possible that in goitre these channels get blocked and then the gland begins to

swell. In 1895 Baumann described Iodo-thyrin. Oswald found thyro-globulin. In 1914 Kendall described thyroxin which is believed by many to be the active principle of the gland. It contains 65.1% Iodine. Ross found no Iodine in the thyroid gland of the wild cat and the dog but it was present in two out of six martens. Crotti concludes that probably thyroxin is an important principle which acts on the general metabolism; that there is also a phosphorus principle which affects the vasomotor and heat centres; a sulphur principle which acts chiefly on the hair and skin; finally an arsenic principle which acts through the nervous system.

Virchow, famed for his work on cellular pathology, made an investigation into the prevalence of goitre and cretinism in Lower Franconia. He held that the nature of the water was the essential factor in the aetiology of endemic goitre but he believed the determining factor to depend on the geological formation from which the water came.

Hirsch, in his summing up of his views on the geological

question in relationship to goitre says that no geological formation precludes the possibility of goitre or cretinism, and that both diseases are more prevalent on the older formations.

An historical account would be incomplete without reference to the great work of R. McCarrison in connection with the aetiology of goitre and his microbic theory and the more recent report of Sir James Berry concerning the causation of endemic goitre. McCarrison (Etiology of Endemic Goitre) says "the cause of endemic goitre is a micro-organism that finds its home in the intestine of man, and there creates a toxin which so influences the thyroid gland that it undergoes enlargement which is the dominant symptom of this infection". Sir James Berry, on the other hand, maintains that the causative factor in endemic goitre is one of the mineral ingredients of drinking water. In his Hunterian lecture reported in the British Medical Journal, February,7th, 1926, p. 269, he states that minute particles of inorganic mineral matter, probably calcareous, suspended in water, if not the cause of goitre, is a necessary

accompanying factor.

The work of Marine, Kimball and Lenhart has made it clear that whatever the causation may be it is undoubtedly contingent upon some disturbance in the Iodine supply. As a prophylactic Marine and Lenhart suggested two grains of Sodium Iodide daily for a fortnight every six months. Klaniger of Zurick found that five mgm. Iodine weekly throughout the year was equally effective. The Swiss Commission so impressed the government that the addition of Pot. Iodide to table salt was made compulsory.

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SECTION 3. A.

Geographical Distribution.

The distribution of simple goitre extends over almost the whole of the inhabited earth but everywhere in more or less narrowly circumscribed spots. Ancient writers knew of its occurrence in Lombardy, Thrace and the Appenines in their day. Caesar spoke of the frequent occurrence of big neck as one of the peculiar characteristics of the Gauls. The origin of the term cretin shows the familiarity of the Romans with this disease, for it is generally held that they had originated this expression of contempt by calling the myxoedematous idiots "Christians". More modern observers noted its existence amidst mountain ranges as distant one from the other as the Urals and the Pyrennes, on the icy steppes of Siberia, and the burning plains of India, in heights thousands of feet above sea level and among the inhabitants of ocean-girt islands. It equally affects the mild Singhalese and the fierce dyaks of Borneo, the white

and the black races, and it is an established fact that the yellow races are far from immune. Goitre is usually associated with mountain ranges although not by any means confined to these. In this connection the Alps, the Appennines, the Rocky mountains, and the Himalaya area of India enclose many centres of goitre. In our own country endemic centres are found east and west of the Pennine Range and in relationship to the Mendip and the Cotswold hills. Simple goitre may be sporadic, endemic, or epidemic. It shows fluctuations in its distribution. It may appear in a district which previously had enjoyed immunity and it may disappear from a region where for a long time it had been endemic. Entire districts are sometimes so intensely affected that a large proportion of the inhabitants as well as the domestic animals exhibit enlarged thyroids.

On European soil there is no higher endemicity to be found anywhere than amidst the western and southern slopes of the Alps. In Switzerland, and in every place where cre-

tinism exists, there is also a considerable number of goitres to be found, but even where there are few or no cretins to be seen goitre may be fairly prevalent, as for instance in the cantons of Grisons, Schaffhausen, and Geneva. The valleys of the Rhone and its tributaries are highly endemic, so also along the Reuss and the Aar. Goitre is especially intense in the Black forest, in Freiburg north of the Rhine, in Argovy, and Berne. No canton is immune. Bircher says that in districts on the right bank of the River Aar 15-30% of recruits are goitrous. The higher parts of the Alps (Berry, B.M.J. 1891 pp. 1269-1273) are less affected than the lower. Goitre is more often found at the foot of a hill than the summit. Bircher (Der endemische Kropp, A. Bircher 1883) reports 80-90% in Berne. It does not occur in the most exposed parts but in the deep valleys upon the slopes of the mountains. Endemism is intense in valleys radiating from Mt. Blanc into Lombardy, the maritime Alps, and the Basses Alpes. The canton Uri is highly affected, especially in the valley south of Lake

Lucerne, at Flaelin, Altdorf, and Attinghausen. In this canton there are 9 cretins for every 1000 of the population. In the Vallais province there are 6 cretins per 1000 of the population, and in Berne 4.2 per 1000. In Vallais cretinism is most frequent in the upper part of the Rhone valley, as for example at Martigny, Fully, Saillon, and Sitten. In the canton Grisons it is found chiefly in the district of the Vorder Rhein, in Kustris, and Disentis north-east of the St. Gotthard tunnel. Some of Lake Constance goitre is endemic in Appenzell, in the communes of Grub, Reute, and Heiden. In the canton Glarus, lying between the Todi chain on the south, Lake Lucerne on the west, and the Lake of Zurick on the north, goitre is endemic in Linthal, Sernfrahl and Kranchthal. The endemicity extends from Basel canton to the Lake of Constance including Berne, Neufchatel, Frieburg, and Vano. It occurs on the south-east of the lake in the Rhone valley especially in the districts of Chateau d'Air and Ormonds as for example at Sepey, Rossiniere, and Rougemont. In the canton of Aargau the disease is most prevalent in Aarau and Lenzburg and at the confluence

of the Reuss and the Limmath in Altenburg, Reuss, Gelunsdorf and Vogelsang. In 1913 a most thorough investigation was made into the goitre prevalence in this canton the results of which were detailed in a considerable work issued from the Health Institute at Zurick (Th. Deterle & Hirschfeld L. & Klinger R. Epidemiologische Untersuchlungen uber den endemischen Kroff Arch. p. Hyg. 81, 128. 1913).

South of Aargau lies the canton of Lucerne and here the endemic is most marked in the districts of Zarsee, Willisan and Entlebuck, especially at Romoos.

Italy.

At Aosta situated at the foot of Mt. Blanc goitre is present among about 30% of the population. It is found in the valleys of the Alpine chain which traverse Piedmont and Lombardy especially along the valleys of the Dora, the Po, and the Adda, and to a lesser degree the valleys of the Sesia, Ticino, and Adige. Bellino and Udine in Venetia are much affected. Between the River Adda and River Mincio lie Lodi and Cremona in which the endemicity is 30 to 80

per 1000 of the population. These all lie north of the River Po. South of this river we find Voghern, Piacenza, and Parma, where goitre is not nearly so severe, affecting only 0.7% of the population. At Val Tellina, in the province of Sondrio, the prevalence equals 26.3%; at Crema 18.2%; at Saluzzo 17.9%; at Bremo in Brescia 17%; at Salo and Chiasa 16.3%. Goitre is also found to a less extent in Bergamo, Lecco, Susa, Pinserato, and at Chesone. For cretinism and idiocy 1.07% of those presented for examination were considered unfit for military service at Aosta. Oswald says that in Switzerland 7% of the recruits are annually rejected on account of goitre as well as 2 per 1000 of drilled soldiers. In Italy 3% of the conscripts were rejected from 1859-1864 on account of goitre or cretinism. Centres for goitre and cretinism also exist in the northern slopes of the Appenines. Goitre also is present in Umbria and Ahruzzi.

France.

The French Commission 1863-1874, according to Kimball

(one of Crile's associates), reported half a million people in France suffering from goitre and 120,000 from cretinism. Baillarger (Rapport de la Commission d'enquête sur le goître and le crétinisme en France. Paris. 1874) reports 370,403 persons above the age of 20 years suffering from goitre. The headquarters for goitre and cretinism in France are the provinces of Hautes Alpes and Savoie. Endemicity is also high in Basses Alpes, Hautes Pyrénées, Haute Savoie, Isère, Ardeche, Drôme, Alpes Maritimes, Arriège and Haute Garonne touching the Pyrennes. There are a few centres in Lot and Avignon, in Hautes Loire, Puy-de-Dome and in Vosges in the north and Pyrénees-Orientales as it slopes to the mountains. The endemicity both for goitre and cretinism is high according to Hirsch in Lower Alsace along the valley of the Rhine in the plain between the Rhine and the Ill in the valleys of the Vosges but in more recent times the percentage is much lower. It is also diminished in Lorraine. In Jura

west of Lake Geneva the goitre endemicity is high but there is very little cretinism. In Savoie the valleys of the Maurienne and Tarantaise are most highly affected with 22.7 and 14.5 cretins respectively per 1000 of the population. In the Hautes Pyrenees the valleys of Luchon Bigorre and Lavedan are the chief centres in this district. In Oise goitre occurs around Compiègne. Cases are found at Rouen.

Spain.

Goitre is endemic along the villages lying in the valleys on the southern slopes of the Pyrenees corresponding to the French department of Haute Garonne. Endemic spots of goitre and cretinism are found in the valleys of the Cantabrian mountains both in Asturias and Galicia, in New Castile and Estremadura divisions in the valleys of the Sierra Nevada and Sierra Morena as well as in the frontiers between Estremadura and Alemtejo in Portugal.

Austria.

The Alpine provinces of Tyrol and the duchy of Salzburg belong to Austria. The Gastein valley is free from

cretinism but contains much goitre. Previous to 1870, according to Graf, (Lancet 1912, p.128) Vienna contained much less goitre but with the introduction of a new water supply in 1870 endemicity increased and in 1910 a further increase took place after the addition of more springs to their water supply. In upper Austria goitre occurs along the banks of the Danube. In Lower Austria it occurs along the Danube valley and the valley of the Leitha. Both goitre and cretinism are prevalent in Styria and Carinthia. In Carinthia 9 per 1000 of the population are cretins and in Styria 7 per 1000. The valley of the Drave is free from goitre and cretinism, nor do these diseases occur in Crotia nor Dalmatia but goitre is found on the slopes of the Carpathian hills and is endemic amidst the Transylvanian Alps.

A recent investigation in Austria (Health of the School Child for 1925. p.132) has shown that in Vienna and the provincial capitals approximately one half of the children show slight or moderate enlargement of the thyroid while in 1.9% the enlargement is classed as "marked".

Hungary.

Goitre occurs in the department of Grosswardein, in Zips, Gomer, Bars, Neutra, Pesth, Raah and Wieselburg. It is present on the eastern spurs of the Norican Alps. Sporadic cases are to be found throughout Hungary. Goitre is endemic in Galicia in the northern slopes of the Carpathians.

Southern Germany.

In the earlier nineteenth century Lower and Middle Franconia were centres of cretinism but now fewer cases are seen but cretins are still to be found at Iphofen, Hellenitzheim and around Uffenheim and Gerolzhofen. In the valleys of the Inn, Alz, Salzach, Traun, Iser and the Wertach goitre may be seen. It is more widely diffused throughout Wurtemburg than in Bavaria. Cretinism occurs in Baden where 3.9% of the recruits were annually rejected on account of goitre. There are minor centres in the Palatinate and the Grand Duchy of Hesse. In the centre and in north Germany cretinism is hardly to be found but goitre is present in Wiesbaden (near Frankfurt) in the Rhine valley, in the Westerwald

(west of Hesse), on the slopes of the Taunus (north of Wiesbaden), and in the valleys of the Aar, the Dille, and the Maine.

Belgium.

The endemic occurs in a few southern districts but is rare on the coast. Very little goitre is to be found in Norway and Denmark, but in Sweden one centre is well-known, namely a few villages in the neighbourhood of Faluh. Minor centres are also found in the mountainous districts of Westmanlandstam.

Russia.

Hirsch (Handbook of Geographical and Historical Pathology Vol.2. p.144 of the Sydenham series) remarks that goitre is to be found on the shores of Lake Ladoga, east of Moscow at Vladimir around Nishni Udinsk on the Uda and along the slopes of the Urals in the government of Perm. Conscription returns for 1893, 1894, and 1895 reveal the fact that the districts lying between the Volga and the Ural mountains is the most goitrous, 16 recruits out of about 20000 men

being rejected by the government of Ufa, 11 out of 20000 in Samara, 37 out of 20000 in Perm (F.G. Clemow 1903 Geography of Disease pp. 170-179).

In the Balkan Peninsula cretinism is found in Montenegro. Goitre is endemic in Roumania, in the territory of Moldavia and Walachia. Goitre is not common in Constantinople but it would appear that it is to be found among the "Lamals" or street-porters.

In Greece goitre is known to occur in two villages in the mountains.

Asia Minor.

In Asia Minor and Mesopotamia goitre centres are met with but Syria, Arabia, and Persia have been stated to be free. As regards Turkestan, Bokhara was stated to be free by Hirsch but to-day goitre is common in this district especially at Kalai Khumba where there is scarcely a family free from this disease. The same is true of a place called Karataj where according to Grekof goitres grow to an enormous size. The Turkoman of both Russian and Chinese Turkestan suffers to a

great extent. Racendonck (Report of Leprosy Conference Berlin 1897) reported that at Yarkand and Kashgar (both in China) and Khokan (in Turkestan) goitres of great size are met with.

Siberia.

Goitre is widely diffused. It occurs especially in the government of Irkutsk, in the valley of the Lena and its tributaries on the slopes of the Altai mountains, in the government of Tomsk along the river Yenisei, and on the Chinese frontier beyond Lake Baikal. Sir George Simpson (Narrative of a Journey round the World, 1847) says "as we advanced through Siberia the very disagreeable complaintgoitre became more prevalent". Kandaratski (7th Conference of Russian Physicians 1899) said he found goitre all along the River Ural.

Goitre occurs also in the Caucasus area especially in Trans-Caucasia but is unknown in Stavropol, Kuban and Terek.

India.

The endemic zone in Central Asia begins in the vale of

Cashmir in the upper basin of the Indus and extends through the mountainous part of the Punjaub and the provinces of Garwhal and Kumaon to Nepaul and Bhutan. Goitre prevails throughout the Himalaya mountains, the Burrail Benrail hills, and the Salt Range. In the Himalayas goitre is more prevalent on the east, where the vegeatation is luxuriant than on the west, where there is much desert land. On the east it is especially in the area bounded on the north by the mountain range, on the east by the Brahmaputra river, and on the west by the river Gogra, that the endemic is highest. On the west goitre occurs along the Chenab as far as Mooltan. The eastern triangle is dotted over with rivers, lakes and marshes, which MacNamara (Himalayan India 1880) considers a feature of considerable aetiological significance. In the Dacca district Dr. Taylor reports that splenic enlargements, elephantiasis, and goitre are common, especially in localities where the people use stagnant water for drinking purposes. In north Bengal goitre and cretinism occur in the Rungpore district, especially along the banks of the

rivers in this neighbourhood. In the province of Behar Dr. Macdonald says the inhabitants are all more or less liable to have goitre and hypertrophied spleen. Dr. Gayer describes the district as altogether unhealthy - marshes and low lands abound; the vegetation is luxuriant. Tirhoot is as bad as can be. Its water supply comes from very unsatisfactory wells and dirty tanks subject to contamination by the foulest surface drainage; they are full of rotting vegetation; the people wash and drink from the same source; human corpses and animal carcases are disposed of by casting them into the river. The people are dirty in their habits, and the villages are heaped with refuse, whilst each man preserves his own peculiar dirt by the help of the thick screen of vegetation with which he surrounds his hut. In Oude goitre is reported by Dr. Higginson as common at Kheri and Singahi and by Dr. McClelland at Kumaon. Dr. Stoliezka found it at Sutlej. In the Peshawar valley goitre is practically unknown. It is rare in Rajputana and the plains of India. In some parts of Burmah it is unknown as at Arakan

but considerable centres are to be found along the Iriwadi and Tenasserim divisions according to Davidson. According to Bennet (Ceylon and its Capabilities 1843) goitre has been prevalent in Ceylon.

Malay States.

In the Kwala Kangsa district of Perak goitre is endemic. According to Rasch it is rare in Siam. Both goitre and cretinism occur in many parts of Sumatra. Goitre is common among the hill tribes of Tava (Kohlbrugge) and among the dyaks of Borneo (A.T. Sloan. Edinburgh Med. Journ. p. 1004). Mr. Marsden (History of Sumatra 1811) speaks of the hill tribes as subject to "monstrous wens from the throat" due, he thinks, to cold morning mists.

Goitre is not unknown in Cochin China.

China.

Goitre is endemic in the northern provinces. Morachi tells of its presence in Pekin. Dudgeon (Glasgow Med. Journ. July 1877 p331) states that he found goitre common in north parts of China. It is endemic in the Szechwan and Yun-nan

districts and at Teheto. It occurs also on the Siberian frontier.

Africa.

Hirsch (Handbook p.148) quotes authorities for stating that the coast was free from goitre but the endemic occurs in the Abyssinian plateau, in the slopes and valleys of the Atlas mountains in the mountainous parts of Morocco and in the basin of the Niger. It occurs round Lake Tanganyika, in the valleys of the Great Soudan in Madagascar and the Azores. (Livingstone found goitre at Lopere and Kebuire in Central Africa). Cook reports the prevalence of goitre in Uganda. Mungo Park (Travels in the Interior of Africa I799) writing of the diseases of the Mandingoes on the banks of the Gambia maintains that goitre was common at this date in some parts of Bomballa.

North America.

Goitre is well known in the Hudson Bay territory, on the banks of the Saskatchewan and at the head waters of the Peace River. Professor Osler made an inquiry into the

places stated by Hirsch to be goitrous and he found that in some of these districts the disease had become rare and in others extinct (Journal of Medical Science, Nov. 1893). At present goitre is not uncommon in Quebec. It is endemic along the banks of Lake Ontario and Lake Michigan. Osler says cretinism is nowhere endemic in North America although sporadic cases occur. St. Lager found goitre prevalent in the States of New York, Ohio, Virginia, Michigan, Kentucky, Tennessee, Maine, Vermont, Connecticut, Massachusetts and New Hampshire. In 1800 B.S. Barton , (A Memoir concerning the Disease of Goitre as it prevails in different parts of North America 1800), spoke of goitre among the American Indians living along the shores of Lake Ontario and Erie. E. L. Munsen, (The Occurrence of Goitre among the Indians of the United States, New York Med. Journ. 1895 lxii 513), describes centres in the Rocky Mountains. F.J. Shephard, (Enlargement of the Thyroid Gland or Goiter Report of Commission of Conservation of Canada Dec. 1918), said the goitre incidence was great in British Columbia

and Alberta. J.G. Adami, (Etiology and Symptomatology of Goiter, Montreal Medical Journal, 1900 xxix 1-17), noted the endemic in the valley of the St. Laurence. Marime found the disease widely disseminated all along the Great Lakes. The War Departmental Report for 1920 stated that of 2,510,791 men examined for military service 11,971 had simple goitre and 8647 suffered from exophthalmic goitre.

Cretinism is endemic in Mexico. Goitre is prevalent throughout Mexico, Guatemala, San Salvador, Nicaragua, and Costa Rica. Marco Polo, the famous Venetian voyager, in chapter thirty-five of his "Travels" speaks of the people of Yarcan as suffering from swollen legs and great "crops" at the throat.

South America.

Goitre occurs along the Andes as far as Chile. On the Peruvian plateau goitre is endemic. Cretinism has been present for a considerable time and in the time of Paul III it had reached such a degree that it required nothing less

than a papal bull to convince the missionaries that the cretins of this region were human beings and had souls to be evangelised. Along the valley of the Rio Magdalena goitre is endemic. In Maraquita Foote found hardly a person free from goitre. In Brazil the greater part of that country is affected, more especially the centre and the south. The river that divides the provinces of Corrientes and Entre Rios is called the Guay-qui-raro or the "thick-neck-maker" by the Indians. Goitre had made enormous strides in South America especially along the river Magdalena where it was formerly unknown. The thyroid affection of Chagas is exceedingly common in Brazil. In Salta in Argentina goitre has been known for many years. It has become endemic in Goyaz and in South Brazil more particularly the provinces of St. Paul and Sainte Catherine. Dr. Smith, (Edinburgh Medical Journal 1842), refers to goitre in the central valleys of the Andes, chiefly among the white settlers.

<u>New Zealand</u>.

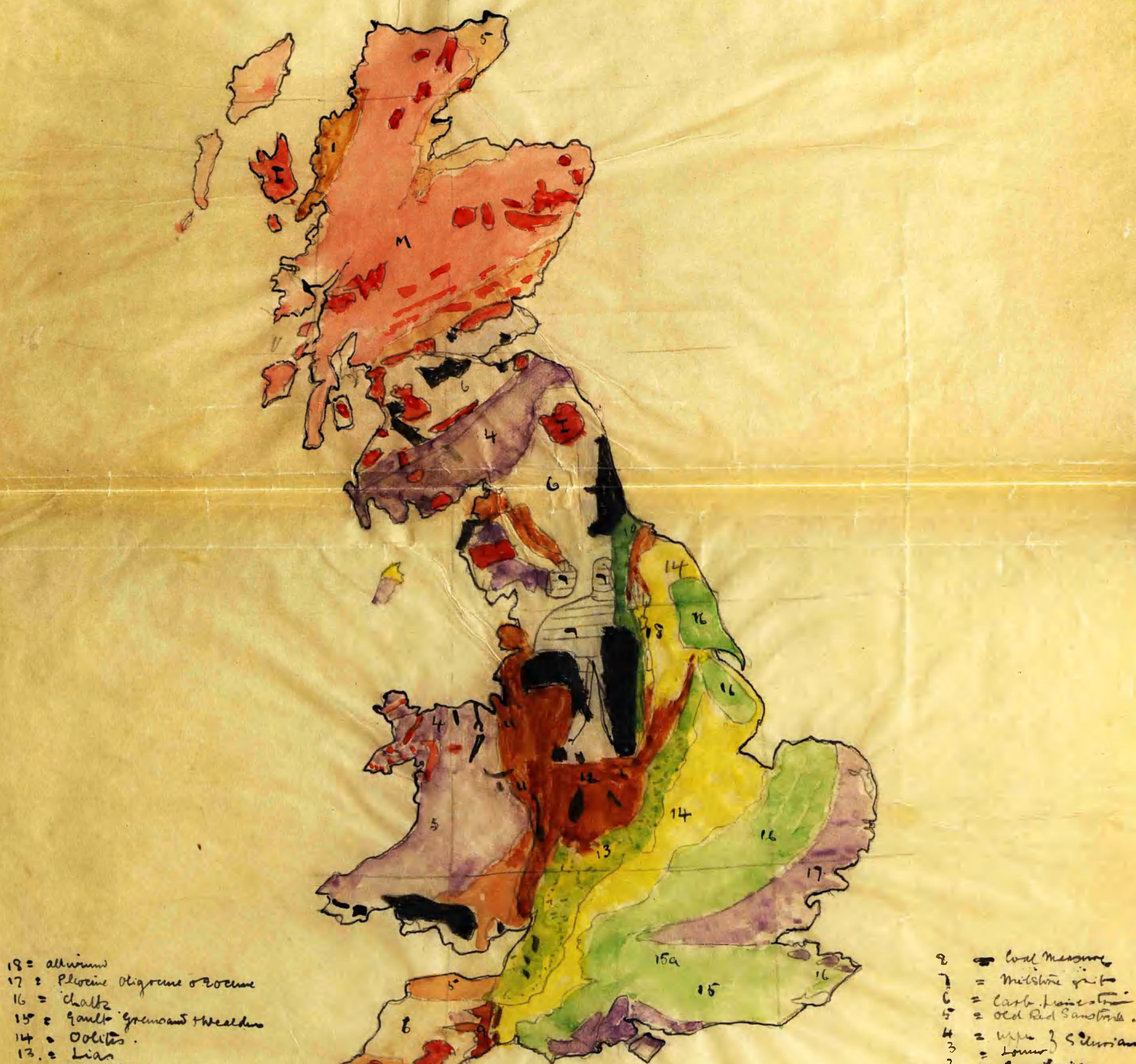
Although goitre is not prevalent in the North Island,

it is found in the South Island, especially at Christchurch (McCarrison Proc. Soc. Exp. Biolog. 1926 xxiii pp 494-496). In the Maternity Hospital at Christchurch 60% of the mothers were found to have enlarged thyroids and 8% of the babies. There was evidence ("Endemic Goitre in New Zealand" Hercus, Baker and Carter, Journal of Hygiene, Vol. XXIV, Dec. 1925, pp.321-402) that in some cases the goitre had been sufficiently large to interfere with the rotation of the babies' heads during labour. They found that as a rule the goitre diminished rapidly after birth even without any special treatment.

Amongst children they found no evidence of cretinism nor any definitely myxoedematous people but they noticed mental dulness, adiposity and thickening of the skin. In Canterbury 60% of the school children had goitre.

Australia.

Although goitre does not occur to any great extent in this country A.E.Taylor (Lancet 1903. P 1324) reports a few cases at Outtram where the water supply is rain-water.


18 = alluvium
17 = Pliocene Oligocene & Eocene
16 = Chalk
15 = Gault Greensand & Wealden
14 = Oolites.
13. = Lias
12 = Keuper
11 = Bunter.
10. = Mag. Limestone
9 = Red Marl.
8 = Coal Measures
7 = Millstone grit
6 = Carb. Limestone
5 = Old Red Sandstone.
4 = Upper } Silurians
3 = Lower
2 = Cambrian
1 = Torridonian
M = Crystalline Schists
I. = Igneous.

Scotland.

Saint Leger, (Etude sur la Cretinisme et la goitre endemique 406-407), says goitre and cretinism are much more common in the south than in the north but his records for mental deficiency in Scotland were the reverse to his findings for goitre for he stated that there were 2603 idiots in the highlands and only about a third of this number in the lowlands. Dan McKenzie, (Glasgow Med. Journ. 1899 pp15-24), states that the endemic centres are few in number, small in superficial extent and of a mild type. Marshall, (Edin. Med. Journ. 1832,) records goitre in Perthshire. It is found in the East of Arran. I have seen a few cases in West Lothian. In the south, goitre is specially common along the valley of the Nith. Mitchell counted 93 goitres along the north valley of the Nith. Chalmers and Grierson (Saint Leger. p.406) found goitre at Thornhill amongst the female population. Kay observed goitre at Sanquhar. Jackson says in 1897 goitre was still

common in Sanquhar but that the tumours were small and caused little or no inconvenience.

Endemic goitre occurs along the Clyde valley, particularly in its middle and upper reaches. The maximum intensity is in the coal districts of Larkhall, Dalserf, Stonehouse, Wishaw, and Carluke; also in the agricultural districts of Strathaven, Blackwood, and Lesmahagow. It dies off abruptly at Larkhall. In Hamilton and Blantyre and Bothwell I have found very few cases of goitre and cretinism. It is seen as far up as the Lead hills but the goitres are small. Around Larkhall 25% of the adult female population are goitrous to such an extent that casual observation could not fail to notice the enlarged thyroids amongst the women of the district. The majority of those affected belong to the mining and labouring classes.

Cretinism is rare in Scotland. In fact a similar statement may safely be made about the whole of the British Isles. Sloan reports small endemic centres in Penicuik and Dollar. Goitre is found in Roxburgh, Selkirk, and

GEOGRAPHICAL DISTRIBUTION OF GOITRE

AMONG ADULTS.

ENGLAND AND WALES

Peebles, in Ayrshire on the east where it is contiguous with Lanarkshire, and Dumfriesshire. It also occurs on the west of Berwick and east of Wigtown. Carlyle mentions frequency of goitre in the circle of Langholm. McLeod reports it at Hawick and in the north part of Galloway. Saint Leger reports its occurrence in Arran notably towards Shiskine.

England and Wales.

The Tertiary rocks in this country consist of Pliocene, Oligocene and Eocene formations. (Miocene is not found in England). Tertiary rocks are found in the London basin. A few cases are found around Bagshot. The reports of the School Medical Officer for London show that goitre is not by any means infrequent there. Goitre is present in the villages lying between Aldershot and Chertsey such as Pirbright and Windlesham. These formations are found along the coast through Essex and the east parts of Suffolk and Norfolk. Goitre is found around Beaconsfield in Norfolk, but Berry says he has failed to find it west of

Swaffham. In Hampshire, it is present at Romsey, but absent from Poole, Bournemouth and Lymington. The highest of the "Secondary" group of rocks is the Cretaceous System consisting of Chalk formations above and Wealden below. As is indicated by the map these rocks are found in Hertfordshire and reach through Huntingdon and Cambridge stretching right up to the Wash. Goitre is to be seen at Hatfield, Hitchin and Harham. In Bedford it is found at Luton, and in north Essex at Sible Hedingham and Wethersfield. Goitre occurs along the valley of the Stour, in Suffolk at Cavendish, Melford, Sudbury, and Mayland. Gault is also found in Yorkshire, and many cases of goitre have been found in Driffield. The north and south Downs appear almost clear. On the lower greensand goitre appears at Ampthill in South Bedfordshire, and in the neighbouring villages of Woburn and Ridgemount. In Surrey we find goitre at Haslemere. It occurs also along the Weald fairly uniformly at Cushfield, Hastings, Horsham, and Hadlow. Among the Jurassic rocks goitre is present in

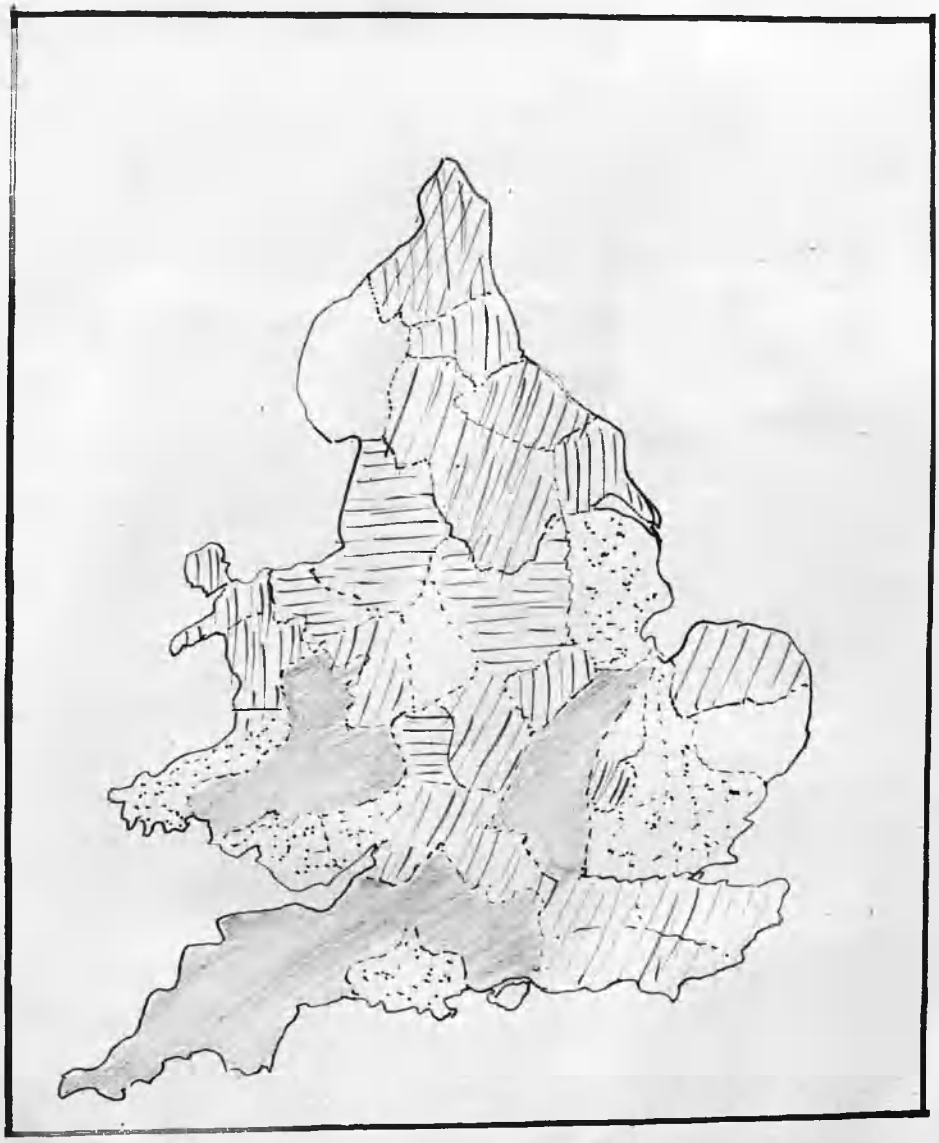
Helmsley in Yorkshire. Although found at Chacombe, goitre is not common on Middle Oolite formation but is present frequently where the Liassic and Lower Oolite rocks reach the surface at or near their line of junction (Berry, Diseases of the Thyroid Gland p.59). These rocks run together from the Bristol Channel to the upper border of the Wash. Goitre is found at Chisleborough, (which was once a seat of cretinism in this country). It is also present at Denham, and at Wooton-under-Edge in Gloucestershire. At Stroud and east of Cheltenham many cases of goitre exist. At Northbach this disease is common. In Warwickshire the endemicity prevails at Avon, Dassett, and Warmington. Beneath the Lias lies the Triassic system consisting of Keuper and Bunter formations. The Keuper is seen stretching from the mouth of the Tees to the mouth of the Exe (Lapworth, Geology, p.292). It attains a maximum width of 50 miles between Leicester and Newport (in Monmouth). It throws off a broad arm to the N.N.W. through Cheshire and Lancashire to Morecambe Bay. In Cheshire, these rocks

are 5000 feet in thickness and contain both divisions of the Triad system. In Nottingham and Yorkshire only the Keuper formation appears. Goitre is rare on the Triads. In south Derbyshire goitre is not found on the Triads at all. It would appear that the endemicity spreading along the Pennine Chain was stopped in its southward spread by this great thickness of rock. It has to be remembered, however, in considering the relationship of geology to aetiology that in any map of a geological kind it is only what appears most superficially that is shown. Sometimes we find formations locally missing, and there is a break or gap producing what is known as an Unconformability which may have an influence on the aetiology at present not understood.

The lower division of the New Red Sandstone is the Permian System. This is represented on the east side of the Pennine Range by Magnesian limestone. It is also found in Lancashire. Manchester rests on Permian Sandstone. It also occurs on the surface in Warwickshire, north part of of Stafford, east Devon, and in Scotland., in Dumfriesshire

and Ayrshire. East of the coal measures of Nottingham magnesian limestone appears and extends as a narrow band parallel to the Pennine hills through Knaresborough and Durham. It consists of Red Sandstone, conglomerates, marls rich in gypsum, rock salt, limestone predominately magnesian in type. Goitre is found at Knaresborough, but not nearly to the extent to which it occurs in association with the carboniferous system. The coal measures form the topmost layer of this latter group, and are well represented in Derbyshire and Yorkshire, and in Lancashire in and around Manchester. Goitre is abundant in the coal-fields, as can be seen at Cromford, Wirksworth, Bakewell, Matlock, Belper, and in villages north of Ashbourne. Along the Dove Dale in North Stafford goitre is frequent. It is also present in valleys amongst the Mendip hills and around Cleveland in Somerset. Goitre occurs in the dales and valleys of the Pennine range both east and west, more commonly south of the Tyne. Along the south side of the Tyne goitre is fairly abundant. On the north side I have seen goitre in the

neighbourhood of Allendale. It occurs also at Haltwhistle. According to Robinson (Goitre or Thyrocele) goitre is common along the R. Rede and on the north side of the R. Coquet in Northumberland. The map indicates the endemicity in Weardale and Teesdale. One cannot help noticing how it follows the valleys in its spread. Of course it is to be remembered that it is in the valleys most of the people live, the high parts being as a rule only sparsely populated. The endemicity then is not so much in the uplands where the rivers have their sources amongst the Pennine hills, but lower down the streams as they cut their way through the hills to make their way to the coast. The goitre prevalence, however, falls off as the coast is approached. In West Yorkshire goitre is seen at Hawes Junction. On the west side of the Pennine goitre is present along the Eden valley in East Cumberland and Westmoreland. It is specially abundant towards Penrith and Appleby where according to Bayers there are very few families where the majority of the members are not goitrous. Goitre prevails at Kendal east of



GEOGRAPHICAL DISTRIBUTION OF GOITRE IN SCHOOL CHILDREN.

ENGLAND AND WALES

Lake Windermere. Along the Ribble and the Mersey goitre occurs in Lancashire at Preston, Bolton, Wigan, and Manchester. Saint Leger observes that it is found at Oldham and many cases are to be seen in the district lying between Oldham and Manchester to which I will refer later.

Incidence of Goitre among Children in England and Wales.

Special investigation into the incidence of goitre among school-children has been set going during the past three years by Sir George Newman, the chief Medical Officer to the Board of Education. In the annual report for the year 1925 Dr. Percy Stokes (The Health of the School-child for the year 1925 pp131-137) finds that "high incidence of thyroid enlargement in adolescent girls forms geographically a curved line extending from the southern end of the Pennine Chain through the counties of Derby, Nottingham, Leicester, Rutland and Northampton and thence in a south-westerly direction through Oxfordshire and the area between the Cotswolds and the Chiltern Hills to Somerset, Devon and Corn-

wall. A secondary band seems to extend from the Chilterns to the Isle of Wight".

Dr. Maurice Campbell has also completed his investigation into the geographical distribution but his figures do not include Cumberland, Westmoreland, Suffolk, and Stafford. (Journal of Hygiene, March, 1927. pp.1-18). The reports of school medical officers throughout England and Wales fall into two categories, (1) Those in whom the thyroid was sufficiently enlarged for increase in the size of the neck to be noticed on casual inspection (without palpation or measurement) and (2) Those in whom it was not so enlarged. Reports were asked for, age thirteen years only, and returns were asked for, giving boys and girls separately.

The incidence at this age for all England and Wales was found to be 4.9%. Goitre appears to be three times as common in girls as in boys, a percentage of 7.2 in the former as compared with 2.6 in the latter. It is twice as common in the country areas as in the large towns and

and more than twice as common on the west as on the east. There is no evidence that proximity to the sea coast is itself a factor of predominant importance. Most of the areas where the incidence is specially high and also where it is especially low are on the sea coast. Hills seem to play a much more important part, according to Campbell, in the geographical distribution of goitre. There appears to be some correlation between the incidence of simple goitre in school-children and deaths from exophthalmic goitre as recorded in the Registrar General's Report. These figures for exophthalmic goitre possibly include all forms of hyperthyroidism including toxic adenoma. If this be true in this country (though it is contrary to what is found in most parts of the world) the need for systematic and early treatment of simple goitre is all the more pressing.

Campbell divides the counties into seven groups according to the prevalence of goitre throughout the country. The highest incidence is found in (a) South-West of England,

with which perhaps Wiltshire and Hampshire should be included; (b) Hereford and most of Wales (c) much of Lancashire Cheshire, Derby and Nottingham; (d) a Midland group comprising Oxford and perhaps Buckingham and Northampton. Complete figures show a higher incidence in the East Riding than in the North and West Ridings. The incidence in Newcastle is 0.8%, in Bradford 1.6%, in Leeds 1.2% as compared with 9.7% in Manchester. Preston has the highest incidence in England with 17.2%. East Lancashire has an incidence of about 9%, whilst the west gives an average of about 2%. These figures seem to bear out the impressions of the incidence in the North of England that I have already referred to in the early part of this thesis.

Incidence of Goitre in Wales.

Among adults goitre, according to Sir John Lynn Thomas, (Gleanings from the Story of the Thyroid Gland, Brit. Med. Journ. Jan. 15th 1927 pp 91-94) is common in counties bordering the sea. It also occurs in patches inland up the

Gwendraeth Valley and around Llanidloes. In the north goitre is found along the vale of Clwyd. He considers that the distribution has little to do with the geological formations underneath but the surface soil is, in his estimation, the factor of prime importance. Among children the percentage at Cardiff is 3.6, at Merthyr-Tydvil 4.1, at Rhondda 5.4 and at Ebbw Vale 14.2. The counties of Monmouth and Glamorgan show an incidence of 1.8%. Hereford stands high at 16.4%, Carnarvon and Merioneth at 8.2%, Montgomery, Radnor and Brecknock 10.9%, Cardigan and Pembroke 1.9%. Llewellyn made an interesting investigation into the distribution of goitre and rheumatism in this country (The Relation of Goitre to Rheumatism, Prescriber, Nov. 1926, Vol.XX N.1. 242, pp 403-408). He found that goitre and rheumatism were closely associated. He found that goitre and rheumatism chiefly affected the female sex in England and Wales; both are more prevalent among the lower classes; both are common in childhood and adolescence, and both are highly sensitive to weather changes.

He found goitre distributed in the valleys of the Pennine, Mendip, and Cotswold ranges. Lancashire is traversed by the Pennine chain and the incidence and mortality from acute cardiac rheumatism in Lancashire is the highest for all English counties, being 101.6 per million of the population. In Norfolk the incidence and mortality for rheumatism is 52 per million and here the goitre figure is low, being 3.7 per cent according to Campbell. In Glossop Milligan (B.M.J. Aug. 28th, 373, E.H.M. Milligan) found that rheumatism occurred in 25% of the goitrous children as compared with 5.5% in the non-goitrous. Again Bristol is partly in Gloucestershire and partly in Somerset, and goitre is endemic in both these counties. Carry Coombs found the death rate from rheumatism in Bristol very high (282 per million). Goitre was found endemic in Somerset, Gloucester, Monmouth, Glamorgan and Carmarthen forming a goitre belt encircling the Bristol channel. Here rheumatism has a high incidence .

Distribution among Manchester Children.

During the past two years I have made a survey of the endemicity in Manchester and district amongst young people. My survey extended chiefly to all ages between seven years and twenty years. In all, 6396 males have been supervised and 7182 females. I have made observations amongst school children in our elementary and secondary schools, amongst pupils in our training colleges, workers in our cotton mills and also among our mixed population. Manchester may be generally divided into three areas:-

1. Moston and Newton Heath extending towards Oldham.
2. Bradford and Clayton on the east towards Ashton.
3. Hulme on the south side of the city on the line to Stretford.

Manchester lies on Triassic marls and sandstone. The superficial deposits are of three kinds. In Moston (no.1) glacial sand extends from Boggart Hole Clough to Prestwick, and across the Irwell to Pendleton and Eccles. District 2 (bradford and Clayton), lies on boulder clay of the drift

type, and has undoubtedly come down from the lake district in Cumberland. District 3 (Hulme) is situated on river gravels and sand, which is found along the Irwell and its tributaries the Cornbrook and the Medlock. Moston and Bradford stand fairly high (an average of 250 feet above sea level) whilst district 3 is low lying, thickly populated and socially of a poorer order.

Amongst school children I found the following results:-

In district 1, 3.7% of the boys and 5.5% of the girls had goitre

" " 2, 8.3% " " " " 11.3% " " " " "

" " 3, 5.2% " " " " 8.0% " " " " "

All ages are included between seven years and thirteen years. All enlargements of the thyroid gland have been included, whether slight, moderate, or considerable. The surprising discrepancy between one area and another is very considerable, but it confirmed what I had previously suspected from previous observation. Those who dwell on clay have the highest endemicity and those on sand of the glacial type stand lowest. Hulme takes an intermediate position as

regards frequency. In connection with this it has to be remembered as M.E. Marsh states in "Surface Geology of Manchester area 1918" that where the predominant feature of the superficial deposits in Manchester is sand, lenticular areas of clay are seen, and where the major deposit is clay, lenticles of sand appear here and there. Another observation I made in my survey was in regard to the Jews in Manchester. I had noticed that whilst many Jewish children attended our clinics for treatment for various complaints, none came because of enlargement of the thyroid. The explanation was soon forthcoming. My survey among the Jews included 1675 boys and 1808 girls and I found amongst the boys 0.4% with goitre and amongst the girls 1.2%. None of these 3483 children were more than slightly affected. In Waterloo Road School where 95% of the boys are Jews and 80% of the girls Jewesses I found two boys and nine girls of Gentile "blood" affected with goitre and only one Jewess with goitre of a fairly moderate size. In Cheetham Central School I found ten cases of goitre but none amongst the Jewish children.

although 25% of the children are of Jewish origin. I will discuss this factor of the endemicity when I am dealing with the aetiology.

The average percentage of those affected with goitre in Manchester, including all ages from seven years to thirteen years, is 4.5 among the boys and 6.5 amongst the girls. For ages below seven years, I have previously found the percentage less than 0.5%. Ages thirteen years to sixteen years yield 8% for goitre among the boys and 13.6% among the girls. Ages eighteen to twenty years give a figure of 13.7. among females. In a large mill in Manchester I had the opportunity of making a survey of 200 female employees of all ages from eighteen years to sixty years and found twenty of them with goitres of considerable size, that is to say 10%. In our thoroughfares I have on many occasions noticed 5 to 10% of enlarged thyroids amongst women of all ages and all classes.

Goitre in Manchester is much more frequent in the female sex. In India McCarrison found goitre of about the same

frequency in both sexes. At no age about five years is goitre as frequent here amongst the male sex. In males there is a gradual rise, according to my observations, up to about seventeen to eighteen years of age and after this the endemicity quickly falls and in adult males only a few goitres are seen and these usually small in size although a few weeks ago I saw a man with a goitre the size of the head of a six months old baby.

The endemicity in Manchester then is higher than is usually supposed. If, as Foedére suggests, goitre is but the first stage on the way to cretinism this increases the seriousness of the endemic. Cretinism certainly is not frequent here. I only know of five to ten cases, but doubtless there are many more. A factor of great importance is put forward by McCarrison (B.M.J. June 1924) when he estimates that 5% of all goitrous mothers are likely to give birth to cretinous, imbecile, or otherwise defective children. In Manchester school area there are 305 imbeciles,

43 idiots, and 68 deaf mutes of school age. There are about 140,000 children of school age in Manchester. Our schools for mentally defective and backward children are always full. Our "Homes" for the physically defective and cripple children are full to overflowing.

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GOITRE AMONG MANCHESTER CHILDREN.

FURTHER investigation into the incidence of goitre among elementary school-children is recorded by Dr. Oswald Taylor in the latest annual report of the school medical officer for Manchester. The number of children examined was 13,578 (6396 males and 7182 females), and all enlargements of the thyroid were included, whether slight (not apparent on inspection) or considerable. No line was drawn between pathological and physiological enlargement. The distribution of goitre was found to vary with the nature of the superficial deposit over the triassic marls and sandstone on which Manchester lies. The endemicity was found highest where the surface deposit is largely clay (percentage incidence 8·8 in boys and 11·3 in girls), and lowest where the surface is glacial sand (3·7 in boys and 5·5 in girls). It was noticed that whilst many Jewish children attended the school clinics for various ailments, none attended on account of goitre. Among the Jews 1675 boys and 1808 girls were examined. Enlargement of the thyroid gland was found in 0·4 per cent. of the boys and 1·2 per cent. of the girls. None of these 3483 children were more than slightly affected. In one school, where 95 per cent. of the boys and 80 per cent. of the girls were Jewish, two boys and nine girls of Gentile stock were found to show enlargement of the thyroid and only one Jewess exhibited any signs of goitre. In another school largely attended by Jewish children ten cases of thyroid hypertrophy were found among the Gentiles but none among the Jews. "It seems clear," says Dr. Taylor, "that the endemicity among the Jewish children is low when compared with the prevalence among Gentiles living in the same neighbourhood attending the same schools and drinking the same water. Many of the Jewish children in Manchester are of Russian origin, and they eat rye bread of a dark coarse texture. It appears, moreover, that they eat more fish and poultry but less beef than their Gentile neighbours. The more indigestible pork they eschew on religious grounds. The pregnant Jewess is well cared for. Alcohol is not allowed, nor is she supposed to engage in outdoor employment from the beginning of pregnancy till the completion of lactation. As a rule the Jewish child is breast fed."

SECTION 3. B.

Etiology of Endemic Goitre.

Much has been written, a vast amount of investigation has been made, various theories have been advanced dating back to antiquity, yet even to-day it cannot be said that authorities are agreed as to the causation of the malady.

Fifteen centuries before Christ the Chinese blamed water for this disease, an opinion accepted by the Greeks and Romans, as well as the Indians of the western hemisphere. Saint Leger, in his remarkable book, enumerated some forty theories, about twenty of which one way or another are associated with water. The popular belief that the exciting cause of goitre is to be found in drinking water is shared by many experimenters, but there is great diversity of opinion as to precisely what it is about water that causes goitre. In different regions rain water is used for drinking purposes, and those who employ such a method of

supply are not usually affected with goitre to any serious extent. Distilled water in fact is sometimes advised (Lancet 1903, pt.2. p.493), as a means of treatment, its influence of course depending on its purity and freedom from contamination. Rain water however may result in goitre when conditions such as Spurway describes are allowed to exist. In a certain hamlet (B.M.J. 1906. pt. 1. p1037) among the Chiltern hills, the rain water was stored below ground under most unsatisfactory conditions and those who partook of it developed goitre. Many other factors suggest water as at least one important factor in the causation. In an epidemic among soldiers at Clermont (Lancet 1903 pt.2. p.340), only those who drank of the local water supply were affected, whilst those who restricted their fluid to wine escaped. Dr. Graf again (Lancet 1912 pt. 1. p. 128) tells us of certain springs which young men were in the habit of visiting when due to be called up for military service. After four weeks' treatment they were fairly certain of being

rejected owing to enlargement of the thyroid gland. A very clear evidence of the influence of drinking water in relation to causation is seen where after the introduction of a fresh water supply goitre breaks out in a place previously free from the endemic, (as occurred at Fully and Saillon as recorded by Chatin). Conversely, a village afflicted with goitre may become free from goitre by a change of water supply, (as occurred in Blegny commune as recorded by Hirsch). McCarrison reports an interesting case in Ireland, which indicates a polluted water supply as the causation of goitre in this particular instance. In South Antrim he tells of a boarding school in an endemic area and of two national schools in the same neighbourhood. The water supply of the former was clear spring water issuing from chalk, and great care was taken to guard it from contamination. The water supply for the national schools came from wells grossly polluted. He found that 10% of the children from the national schools suffered from goitre but not a trace

of this malady was to be seen amongst the boarding school children. This case is interesting and certainly is suggestive but we must not lose sight of the fact that the diet of the boarding school children would be as well looked after as their water supply. Again in the alluvial fan of Gilgit there are nine villages situated one below the other along the Girgal stream. The first eight get their water supply from the river but the ninth has a supply of spring water. The first eight villages are affected with goitre in gradually increasing degree from above downwards but the ninth village is quite free from goitre. It seems then that the freedom of this ninth village from goitre is due to its freedom from an obviously polluted source of water supply. The other factors are the same for all nine villages.

Climate and Atmospheric Conditions.

Others again have alleged climate and atmospheric conditions as productive of goitre. As a matter of fact goitre

can appear amid the ice floes of Arctic and Antarctic water, (as Captain Cook's crew learned), and amongst the dwellers in tropical lands. Goitre is found in the dusty desert, and also where rainfall is considerable. The association of goitre with heavy mean rainfall may be a consequence of the association generally of goitre with hilly districts. Some have suggested absence of sunlight as an etiological factor of importance. Certainly Manchester has a high humidity. It owes its prosperity as the centre of the cotton trade largely to this factor. Again we are badly off here as regards sunlight - our daily mean averages about 2.8 hours per day as compared with 5.12 in the Channel Islands. Cohen and Ruston (Industrial Smoke Study of Town Air 1912) in Leeds showed that 41% of the sunlight was cut out in industrial centres as compared with rural districts. In Manchester Mr. E. Arden showed that at Davyhulme (outside the city) the light received was 2.36 times that received in the centre of the city. But want of sunlight can hardly

be considered the only factor or even the main factor in the etiology, for if it were so we should expect to find goitre highly endemic among miners, but as a matter of fact in this country where goitre affects mining districts it is chiefly the female section (who do not work down in the pits) of the community who are the sufferers. Pit ponies do not seem to suffer from this complaint, nor can it be said that goitre is more prevalent in towns than in country districts. Still, sunlight may play a part in the breaking down of organic compounds of Iodine and the liberation of free Iodine, which is thought by some to be of prime importance.

Thursfield (Lancet 1885 pt.1. p.1074) enumerates six factors in the etiology of goitre. He says that those who live in hilly districts are constantly exposed to sudden alterations in the barometric pressure and to sudden alterations in their circulation where inclines and declines are at all sharp. He believes that the thyroid gland is a provision of nature for meeting sudden alterations in

the brain circulation. He records the popular belief that goitre may appear suddenly after great mental excitement. He suggests that goitre is due to a permanent expansion of an organ normally distensible for physiological purposes. He voices the opinion held by some that carrying weights on the head, or the wearing of a tight collar by a soldier or the bearing of heavy weights by the head and neck in the case of the Constantinople street-porters, may produce goitre. He tells how at one period the women in a certain district employed in connection with the coal and iron trade, carried heavy weights on their heads, and were much affected by goitre. Some years later, after this custom had gone out of vogue the women suffered to a much less extent from this complaint. After all, there are relatively few soldiers, relatively few individuals who carry weights on their head or otherwise impede the circulation by any of the methods suggested above who are goitrous, so that at the best this cannot be looked on as an important etiological factor.

Intermarriage again as a causal factor in endemic goitre can be put aside, for although consanguinity doubtless is common in many isolated villages where goitre abounds it is just as common in villages where no goitre can be found.

Mac Namara (Himalayan India) noting the frequency with which goitre was associated with damp marshy soil attributed this disease to a malarial ~~region~~ origin. He considered there was a close relationship between the thyroid gland and the spleen, as he often found both thyroid gland and spleen enlarged in the same individual at the same time. It is of course possible for one person to be suffering both from malaria and goitre at the same time, and evidently this was the case in the circumstances MacNamara describes, for goitre is quite a common disease in many places where malaria is unknown. Dr. Grasset (La France Medicale July 15. 1898), has described a haematozoon which he considered the explanation of goitre, but others have not been able to confirm his views. Klebs (Weber die Ursache des

Kroffes Prag. Med. Wochensche 1877 ii 45), found in the waters of Salzburg naviculae which he considered the cause of goitre. Bircher found diatoms and rod-shaped micro-organisms in goitrous waters, but failed to detect any of these microbes in the thyroid gland. Goitrous glands were generally found sterile by Professor Kolle. Gelbride noticed the streptococcus vermiformis, but none of these workers have been able to prove that their findings have any relationship to causation. Riviere noted a cladothrix in the parenchyma of a goitre but this appears to be an unusual finding and has not cleared up the question of the etiology.

There are many other theories suggested in Saint Leger's treatise which are only of historic interest, such as the radio-activity theory of Baumgarten, onanism, licentiousness and the alcoholic theory of Tiedemann. Schwabbe maintained that absence of Sodium Chloride might explain goitre, and Eulenberg found that in the Coblenz circle where the water supply was poor in chlorides goitre was prevalent, and where

the chlorides were abundant there was no goitre (Archiv. für gen. arbeiten 1860 iv 34). The presence or absence of many more mineral ingredients in drinking water have been brought forward as an explanation of goitre, but proof was wanting. Saint Leger considered simple goitre to be due to the presence of Iron in water used for drinking purposes. The occurrence of goitre upon the blue marls of the Wealden and gault (the blue colour is due to the presence of Iron) supports this view. Again goitre in England is often associated with chalk which contains glauconite, a hydrous silicate of Iron and Magnesium, and marcasite, a readily decomposable form of Iron bisulphide. On the other hand goitre is found where not a trace of Iron can be found in the drinking water. If Iron was a cause of goitre it would scarcely be suitable for medicinal purposes, yet probably there is no drug more used from the whole pharmacopeia. Saint Leger quotes Bouchardet and Claude Bernard in support of his condemnation of iron for medicinal purposes, and he appeals to the testimony of Paracelsus

and Agricola in support of his view. (Saint Leger Etude... pp 446-450). Now many goitrous wells are loaded with Iron; on the other hand many of the waters of Derbyshire are free from a trace of Iron, although goitre is so abundant there. Manchester water is a clear water coming from Lake Thirlmere (lying around volcanic rock of the Borrowdale series) and a second supply from Woodhead. The water is soft, is free from Iron and contains only a trace of free and albuminoid ammonia. Wood head water contains twice as much solids as Thirlmere water. Water however carried over such a long distance is liable to accidental contamination through a bad or insecure joint. Where water is stored in the house there is a possible source of contamination. Lately I found an overhead supply of water loaded with iron due to the gradual action of the water on an iron rod suspended from the tank. There was a layer of iron half an inch thick in places in the bottom of the zinc container. Iron mails likewise may be a means of increasing the iron

contents of a water which is supposed to be Iron free. I have at different times observed that when the cold water is first turned on in the morning it is of a brown colour.

In the north of England goitre has been for generations attributed to the use of hard water for drinking purposes. Whilst, however, some goitrous waters are hard this is not always the case. Wirksworth for example has a water containing only six parts per 100,000 parts hardness and has much goitre. A town such as Sunderland has little goitre and uses a water containing thirty parts hardness. Saint Leger fed two dogs for six months on food containing calcium sulphate and magnesium carbonate in excess, but this failed to induce goitre. Feeding mice however, with food containing excess of Iron Sulphide and Iron Sulphate caused goitre. Dr. Berry and his brother tried calcium,magnesium, potash, soda, and other minerals on guinea pigs but their results were negative. Lustig and Carle (Sall. etiologia del gozzo endemico Lustig and Carle Giorn de R Accad de Med. di Torino. 1890 pp 689-717) got positive results in a horse supplied with a hard water. In Champagne the water

is hard but there is no goitre. Faluh, the single locality in Sweden with goitre, has a water that cannot be excelled for chemical purity. The water of Florence is impregnated with lime but yet there is no goitre to be found in that city. Repin, in spite of so much contrary evidence, insists (Revue d'Hygiene, no.4 and 5, 1911,) that the "hard" theory cannot be discarded since goitre endemicity is so frequently associated with lime and magnesium rocks. Grange too, finding much magnesium in the Alps concluded that Magnesium was the cause of goitre. McCarrison and Hayden however made an examination of the soils in certain of the villages of the alluvial ~~form~~ fan and found that the amount of magnesium, calcium, and iron bore no relationship to the endemicity amongst the natives.

Goitre endemicity has been investigated in relationship to the geology of the affected districts. It was Pliny who said "Tales sunt aquae quales terrae per quas fluunt". Billiet in Savoie found goitre indigenous to argillaceous calcareous schists, but absent from siliceous sandstone, granite, gneiss, and mica. In the Alps Grange found goitre

prevalent over the marls, limestone, and magnesium, hence his view, already mentioned, of the causation of endemic goitre. In Switzerland, Bircher concluded that goitre occurred upon marine sediments of Palaeozoic, Triassic and Tertiary periods. In this country Berry (Diseases of the Thyroid Gland p. 63), has drawn attention to the coincidence of goitre with the calcareous rocks which are so widely distributed in England. It is not only on limestone, but on calcareous sandstone that goitre is found. He states (Lancet Feb.6th, 1926), that in the vicinity of mountains geologically young, as in Switzerland, in which erosion and denudation are in full activity, goitre prevails. In the older formations, such as the crystalline schists of the highlands of Scotland and Norway, denudation is practically over. It is impossible to travel through the west highlands of Scotland and not be impressed by the enormous masses of bare rock with hardly a patch of verdure anywhere. The geological condition is reflected in the water coming from these rocks. In Switzerland the streams are muddy and loaded with

minerals and debris, whereas in Scotland the water is pure, clear and contains no mineral in suspension, as is well seen in the water from Loch Katrine.

Berry concludes that "minute particles of inorganic material probably calcareous in character suspended in water, if not the cause, are at least a necessary accompanying factor". This theory would explain the rarity of goitre in the north of Scotland, its high endemicity in Switzerland and the north of England, its infrequency in Norway, and its abundance in the Himalaya mountains of India. But this theory does not fit in with the conditions that prevail at Faluh in Sweden. Here in Manchester, as has been already mentioned, the water is of a high order of purity yet goitre is endemic. Again, Hercus and Baker (New Zealand Med. Journ. 22:79 April 1923), record an outbreak of congenital goitre in a flock of lambs where the ewes subsisted entirely on grass and turnips, and had no access to water except from rain and dew.

Hirsch concludes (Handbook p. 168) goitre is found on

the oldest formations as granite and gneiss as at Aosta, amidst the Silurian and Devonian systems as in the Vosges and at Salzburg, among the coal measures of Derbyshire associated with Permian rock as in the maritime Alps, the Trias in the Tyrol and chalk as in Norfolk. In fact he says no geological formation excludes the possibility of the occurrence of goitre. Mc Carrison says that whilst it is true that goitre is much more commonly associated with limestone and dolomite in this country, this association is not constant. Goitre can and does prevail on almost every other geological formation from the most ancient to the most modern.

Professor Wihms of Basle has propounded another theory. He says the materies morbi (Lancet 1911 pt.2. p.1346), is an organic soluble substance which can pass through a Berkefeldt filter. Others associate goitre with the ingestion of clay suspended in water or as a result of eating with dirty hands. Forbes writing of the Aymeras of Bolivia (A.S. Ashmead New York M.J. 1895. p.241), said that in

certain parts the Indians suffer much from goitre or "ecotosis" as they call it. They are clay eaters. Clay consists of silica, alumina, lime, magnesia, Iron, Manganese, potash, organic matter and water. Undoubtedly quite apart from the mineral constituents of the clay numberless bacteria would be ingested, and a general intestinal toxaemia would be caused resulting in goitre. That intestinal toxaemia plays a part in the causation of goitre McCarrison has maintained for a long time. He stated that in his opinion goitre was caused by a specific living organism that makes its habitat in the human intestine, where it elaborates a toxin which so influences the thyroid gland that it undergoes the enlargement which is the dominant symptom of this infection. There is much evidence to suggest that goitre, in some cases at any rate, is due to a toxic agent. Blake writing on myxoedema and allied subjects in 1894 suggested that goitre was an intestinal toxaemia. Jaboulay suggested that early goitre might be due to a buccal invasion through a patent ductus thyroglossus. Andriezer (B.M.J. 1893 pt 2 p 678) pointed out the embryo-

logical connection between the thyroid gland and the intestinal canal. It would seem, however, that the toxaemia may be elsewhere than in the intestinal canal. I have noticed that sometimes a goitre will increase during an attack of sore throat or even an attack of furunculosis. The removal of unhealthy tonsils, the extraction of infected teeth and the treatment of constipation, I have found to be followed by improvement in the goitre. Riviere records a case that came under his observation where a goitre increased threefold after quinsy.

By filtering the Girgal water, and ingesting the residue scraped off the candle through which this water was filtered, McCarrison induced goitre in himself in about fifteen days. Other volunteers were subjected to the same test with a similar result. He then tried the effect of submitting the water residue to boiling before giving it for ingestion. He found that in the latter case no goitre was induced. This suggested a living organism as the causation of goitre. Again intestinal antiseptics like

Lactic acid and Thymol had a curative effect in goitre. I have tried Kaolin, Lactic acid and Manganese with encouraging results. This suggests an intestinal toxaemia in goitre. McCarrison made cultures from goitrous faeces incubated under aerobic and anaerobic conditions. He afterwards prepared vaccines which were shown to be curative in recent cases of goitre. All this was strongly in favour of McCarrison's thesis. It has been said that no other theory can account for the total disapperance of goitre from a district where it has been endemic, for its sharply defined geographical distribution, and for the epidemics that have occurred chiefly among soldiers in barracks.

Other workers particularly in America have followed other lines of investigation. As far back as 1820 Coindet reported that goitre could be reduced by means of Iodine. In 1856 Chatin maintained that goitre and cretinism could be prevented by the administration of Iodine. He found Iodine widely distributed in nature, in air, in

water and in the soil. He stated that the higher the position in the Alps the smaller became the amount of Iodine in the air and the soil and the greater the prevalence of goitre and cretinism. In North America, McClendon examined a number of foodstuffs and numerous waters and found that in the districts free from goitre the Iodine was high and where goitre prevailed that the Iodine figure was low. He constructed an Iodine card and found that it corresponded fairly closely with goitre distribution in North America. In Germany Th. von Fellenberg made notable investigations which he has published in the Biochemische Zeitschrift 1922-1925. He noticed in La Chaux-de-Fonds that goitre was rare and at Signau in the Emmenthal district (Switzerland) that there was much goitre. Chemical investigation revealed the fact that at the former place the air, soil, and water had an abundance of Iodine, and in the latter place the Iodine figure was low. He has since examined the endemicity in Aargau and found that at Effingen, where there was very little goitre,

that the Iodine figure was high in water, soil, milk, and eggs. At Kaisten and Hanzenschwil where goitre prevailed to the extent of 61.6% and 56.2% respectively, that the Iodine content was low. This shows in a very striking way the importance of Iodine. The discovery of Baumann in 1896 that Iodine was present in the thyroid gland was followed by the important work of Marine and Williams who concluded (Relation of Iodine to the Structure of Thyroid Gland. Archiv. Int. Med. I 349-384. May 1908) that all thyroid hyperplasias were essentially the same and due to deficiency of Iodine. Marine writing (in Journal A.M.A. 15th Nov. 1926 pp 1463-1464) on the subject of Iodine deficiency said that deficiency might be relative and due to an increased need as at puberty, pregnancy, and lactation, during infections and intoxications, suprarenal injury or to meet and balance a fat or proteid diet. The deficiency might be due to interference with the absorption or to low intake. Marine has shown that so long as the percentage of Iodine in the thyroid gland does not fall below 0.1% of

the dried gland no hyperplasia can occur. It is obvious then that goitre is at least immediately due to deficiency in Iodine, and that this deficiency may be absolute or only relative. McCarrison has shown by his experiments on pigeons that allowing the cage to become filthy the bird developed goitre but this did not happen if the cage was kept clean. The pollution allowed the setting up of an intestinal toxaemia and, as Plummer has suggested, the intestinal bacteria rob the thyroid gland of the available Iodine and so deficiency of Iodine follows and hence the goitre.

It does not seem likely that there is a specific organism in goitre but whilst simple goitre is theoretically due to Iodine deficiency, it is due in practice to a combination of factors, among which the intestinal one is of prime importance. De Querwain (A Contribution to the Study of the Pathology and Treatment of the Thyroid Gland and Goitre) objects to the Iodine theory on the ground that Iodine deficiency does not explain the striking variations

in the endemicity of goitre from village to village, family to family, and among the numbers of one family. The objection can be met by the following consideration - In a family the Iodine need varies with age and the absorption formed. The percentage of Iodine in one village may differ in a striking manner from that in a neighbouring village as regards milk, eggs, water, air, soil, etc.

In regard to the endemicity among the Jewish children in Manchester it is surprising how low the occurrence is as compared with Gentiles living in the same neighbourhood, attending the same schools and partaking of the same drinking water. That so few of them are affected with goitre is in keeping with the popular belief that Jews are not so liable to cancer as Gentiles are. Many of the Jewish children in Manchester are of Russian stock. They eat rye bread of a dark coarse texture rich in iodine and in vitamins. They eat more fish than the average English boys and girls do. The Hebrew child is as a rule well fed. They have fish at least twice a week and they take great care to ensure

that the fish is quite fresh. They never buy fish without carefully examining the gills. They are not particularly inclined to animal flesh but here again they take special precautions to ensure the wholesome condition of their food. Fat and blood, on religious grounds they refuse. The more indigestible pork they eschew. Fat bacon is much sought after by our English people but a Jew would not touch bacon on any consideration. Again a pregnant Jewess is particularly well cared for. She is not allowed alcohol under any circumstances nor is she allowed to engage in out-door employment from the beginning of pregnancy to the completion of lactation. As a rule the Jewish child is breast fed.

That diet is an important factor in the etiology of goitre is well recognised. In 1911 Marine and Lenhert, (Further Observation on the Production of Goitre in Brook Trout) showed a rich protein diet was an important factor in the production of the so-called thyroid carcinoma in trout. In 1912 Chalmers Watson confirmed this finding. (Influence of Diet on the Thyroid Gland. Quart. Journ.

Exper. Physiology v 229). In 1920 McCarrison showed that fats are important in the production of thyroid hyperplasia. In this country Mellanby in 1921 (Abstract. Journal Physiol. LV vii) showed the importance of a fat-thyroid-iodine balance in diet. Carbohydrate in excess does not have the same effect as an excess of fat. In 1922 Marine (The Present Status of the Functions of the Thyroid Gland. Phys. Reviews II 521-551) suggested that thyroid activity was more necessary for the oxidation of the fats and the proteins than for the metabolism of the carbohydrates. Mellanby on the other hand suggests that the unsaturated fats such as the oleates may reduce the available iodine in the diet by uniting it to the unsaturated linkages. The incomplete absorption of these fats in the diet would thus lead to a loss of iodine through its discharge in the faeces.

In 1924 McCarrison (A. B.M.A. Lecture on Goitre. B.M.J. pt 2 p 989) claimed that an excess of calcium in the diet was productive experimentally of colloid goitre. Confinement in dirty cages on the other hand produced hypertrophic

goitre in pigeons. McCarrison advances evidence that faecal contamination of the drinking water is an important factor. In a recent paper (R. McCarrison Experiments in Goitre Prevention) he referred to Sanawar in the Punjab. In 1913 he found that 60% of the girls above 16 years of age at a school in this place had goitre. In 1918 a new water supply was procured from Kasauli. By January 1926 it was reported that goitre was altogether absent among the school-girls. Now it was shown that the water from Kasauli was entirely free from iodine. The school, moreover, is situated in a district where the iodine content of the soil is very high (300–400 parts per ten million parts). Again it was ascertained that there had been no change in the diet in recent years. The conclusion is forced on us that the first water supply was the cause of the goitre. Perhaps the goitre, McCarrison suggests, was due to bacteriological impurity in the earlier water supply. He has not however isolated any causative organism. Rosenow of the Mayo clinic has isolated an anaerobic Gram

positive diplobacillus from excised human glands. He found this organism in 25 out of 32 cases of goitre. (Gleanings from the Story of the Thyroid Gland by Sir John Lynn Thomas. Brit. Med. Journ. Sat. Jan.15th, 1927 pp 91-94).. He injected sixty-eight animals with strains of his diplobacillus (taken from 16 patients who had had their thyroid glands removed on account of goitre) and found that 50% of the animals had developed grave thyroid lesions. Rosenor's work still awaits the confirmation of other workers in the field of thyroid diseases.

In April of this year McCarrison (Lancet April 30th 1927 pp 916-920) described a new type of goitre which he had produced in white rats. It appears quite different from previous types of experimental goitre. Williamson and Pearse consider the goitre produced almost approaching the adenoid goitre of primary Grave's disease. The cause of this goitre is evidently not associated with iodine deficiency. The absence of green vegetables and fruit in a diet containing over 60% white flour and less than 20% protein, even though the amount of fat and salts are adequate, seems

important in the production of this form of goitre. The cause is dietetic. There is an insufficiency of vitamin B. The insufficiency of vitamin B, McCarrison suggests, may cause intestinal stasis and a consequent toxaemia. This type of goitre is not prevented by iodine but by a well balanced diet rich in vitamins.

McCarrison has related the two foremost theories of the causation of goitre, (infection and lack of iodine) by assuming the fundamental importance of lack of available iodine and attributing to intestinal bacteria the role of interfering with the absorption or assimilation of iodine from the intestinal tract. It is disputed whether intestinal bacteria can or cannot absorb iodine. Fellenberg says B. Coli can absorb free iodine in appreciable quantities. This may explain the hyperplasia that occurs in the thyroid gland in infectious diseases (Farrant R. Proc. Royal Soc. Med. Section of Path. vi pt.3. pp.21-48. 1913. 1914. Ibid. vii. part 3 pp. 49-68).

Hercus, Benson, and Carter (Endemic Goitre in New

Zealand and its relation to the soil Iodine. Journal of Hygiene. Vol. 24. Dec. 1925 pp 321-402) consider gastro-intestinal infection a factor of minor importance. Although goitre is very prevalent in Canterbury, amongst colonials, the Maoris, in spite of the fact that they are much more exposed to faecal infection than the other inhabitants, show a low incidence of goitre amongst their own people. With regard to McCarrison's deductions from the goitre incidence in the Gilgit fan Hercus and his colleagues say "We are asked to assume that being far from the sea and at an elevation of 4000 feet, iodine content must be low and that the factor of removal of infection is the determining one". McCarrison had found the eight upper villages had a high incidence of goitre but the ninth village had no goitre. Since the first eight villages got their water-supply from the river whilst the ninth was supplied with spring water McCarrison concluded that the river water was the cause of the goitre. It has to be remembered that springs from igneous rocks often contain much iodine,

(at least sufficient to affect the incidence of goitre). It is possible that the soil around the ninth village differed from the others. It is probable that the scanty soil on this fan consisting of limestone and mica schist to a great extent in the neighbourhood of the first eight villages would be poor in iodine, whereas a village low down on the fan, deriving its water from igneous rock, probably granite or diorite, (but possibly altered basic lava) would also be likely to contain a noteworthy amount of iodine. The clinical constitution of the water supplies must be known exactly before conclusions can be drawn of etiological significance.

Hercus and his colleagues found in New Zealand a very definite relationship between the incidence of goitre and the amount of iodine in the soil. The figures for goitre incidence and soil iodine when plotted as ordinates and abscissae so closely correspond that the resultant curve might be expressed thus:-

$y = \frac{360}{x} + 6$; where y = the percentage incidence

of goitre in school-children and x = the amount of soil iodine in parts per 10^7 of the soil.. These workers conclude that the fundamental cause underlying all secondary factors in the production of goitre is iodine poverty in the soil.

Like rickets goitre is a condition in which the causative factor is not simple. The immediate cause apparently is iodine deficiency. Now the iodine in soil comes from the rocks from which the soil was produced, and from the atmosphere. Atmospheric iodine is derived in part by volatilisation from the soil, and in part by the decomposition of iodine bearing organic matter. Again iodine is also volatilised from the sea, from lakes and from rivers. It is probably also exhaled from volcanic vents. The iodine in the air is brought down by rain into the soil. The iodine in the soil is reflected in the neighbouring waters and the amount of iodine in plants grown on the soil will also correspond to the amount of iodine in the soil. It is obvious therefore that many factors enter into the causation of goitre. Neither geological formation, nor soil compo-

sition, nor the purity and iodine content of the water supplies, the proximity to the sea, the nature of the food supplies nor the dietetic habits of the people can be put aside in the consideration of etiology.

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SECTION 4.

Histology, Physiology, and Pathology.

The Thyroid gland originates from the hypoblast, growing as a diverticulum from the foregut. (Green's Encyclop. Med. & Surg. pt. vi. p.107. J.W. Ballantyne). A depression appears in the mesobranchial fold of His, which deepens to form the thyroglossal duct. This duct can be seen to bifurcate to form the isthmus. The lateral lobes arise as terminal buds. The hypoblast cells form the epithelium of the vesicles whilst the stroma of the gland is of mesoblastic origin. (Halliburton Handbook of Physiology. p.871). The thyroid, says Schafer, (Endocrine Organs. E. Sharpley Schafer p.15) is almost the first organ to become distinct in the human embryo. At the end of one month the human embryo is about six millimetres long, and the opening of the thyroid into the pharynx is closed by the obliteration of the lumen of the thyroglossal duct, but the original opening is marked throughout life by the foramen caecum. "Primarily", says

Marine, (Bull, John Hopkins, Hosp. Rep. 1913 pp.135-141) "the thyroid is a part of the alimentary tract, and in its endostylar form is a digestive gland of great importance through its probable external secretion. In its ductless form it is only the atrophic remnant of its ancestor which, while it has suffered a corresponding distortion of function, still profoundly influences the animal's nutrition through the effect of its probable internal secretion". In 1893 Andriezer (Brit. Med. Journ. 1893 pt ii p.678) suggested that in higher vertebrates the secretion of the thyroid gland acts on the respiratory tissues enabling them to take up oxygen more easily and in this way encouraging the gaseous metabolism.

At the time of birth the thyroid gland is characterised by the absence of colloid, by an abundant desquamation of epithelial cells, and by a considerable development of blood channels. After a few weeks it reassumes its classical acinous structure, which it first obtains at the fourth month of intrauterine life and loses only temporarily at the time of birth. (F. De Quervain. Goitre p. 22).

Murray, however, (The Thyroid Gland in the full time human foetus and in the newly born infant. Brit. Med. Journ. Jan. 1st, 1927 pp 5-8), considers this histological picture to be the result of post-mortem changes. He says that the thyroid gland of the full-time human foetus and also of the newly-born infant appears to be normally composed of small vesicles lined with cubical epithelium and filled with colloid. After death vacuoles appear in the colloid and gradually the colloid disappears and eventually the vesicles get filled with desquamated cells, presenting a solid appearance. Kull, who traced the development of the thyroid gland in the albino rat, (Kull H.A. Development of the Thyroid Gland. Anatom. Rec. Feb.25th, 1926) says that the development of the gland takes place rapidly in the last 3 or 4 days of embryonic life. From the 21st to the 22nd day of the embryonic stage an almost explosive unfolding occurs so that the day before birth the gland is completely folliculated. Eugenie R.A. Cooper (The Histology of the more important Endocrine Organs at Various Ages. Prescriber Vol. xx No.

236 May 1926 pp 74-75) says that during early intra-uterine life the thyroid gland is developing vesicles from solid epithelial cell masses through the intermediate stage of branching tubercles. In the latter half of foetal life the epithelial cells become active, colloid being secreted and stored in the vesicles. This goes on till birth when the gland rests and uses up the colloid previously secreted. Later, its activity is resumed, the cells attaining their full size and secreting capacity. Throughout infancy and childhood secretory activity is marked, and so is absorption, but a small reserve of colloid is always maintained. At puberty, demand for internal secretion is at a maximum and although production is abundant it is rapidly absorbed and colloid storage is at a minimum. After adolescence, although demand is less, the secretory acitivty continues and the colloid store becomes very considerable. During adult life the gland enjoys a period of comparative inactivity. In old age the necessity for secretion does not warrant great activity and the gland retrogresses. The thyroid gland lies in a special compart-

ment of the fascia of the neck, shut off from the mediastinum by a fibrous tissue diaphragm. It consists of an isthmus and two lobes. Each lobe has a hilum, where interstitial tissue dips into the lobe carrying blood vessels, and lymphatics, and dividing the structure into smaller and smaller portions. The ultimate lobules are of irregular form but for the most part are roughly circular or oral in section, and about 0.50 to 100 millimetre, in diameter. (Swale Vincent, Internal Secretions and the Ductless Glands p. 290). Each vesicle is lined by one layer of epithelium which rests on a vascular connective tissue envelope. The epithelial cells lining the vesicles are of fairly uniform size and may be cubical or columnar in shape, but in either case they tend to become flattened out as age advances. The protoplasm of the cells is retiform, and each cell contains a round or oval nucleus. Two types of cells have been described, the "chief" and the "colloid", or, as Langendorff describes them, (O. Langendorff. Arch. pp. Physiol. Suppl. 1889), the "hauptzellen" and the "Colloidzellen". The

"chief" cells are the more numerous, stain clearly, and are fairly granular whilst the "colloid" cells are more opaque and more granular. According to von Ebner these do not represent two distinct varieties of element. The "colloid " cells are but "chief" cells loaded with colloid granules which they discharge by rupture of the cell membranes and reassume the phase of "principal" cells. (Allbutt, System of Medicine). The colloid may equal half the total bulk of the gland. (McCarrison The Thyroid Gland pp 8-11). In the intervesicular space lie groups of cells, the so-called foetal cell masses of Wolffler. (Ueber die Entwicklung und den Bau des Kropfes Beolm 1883). Vacuoles appear in the colloid which may be composed of fat or mucin. The contents of the vesicles completely fill their interior as can be demonstrated in osmic acid preparations. Acetic acid causes swelling of the vesicular contents. With strong nitric acid the zantho-proteic reaction is obtained. Copper sulphate and potassium hydroxide at 40° give the violet biuret reaction. Adamkiewicz's reaction is obtained by treating with sulphuric

acid preparations that had been previously treated with acetic acid.

Williamson and Pearse have brought forward evidence which suggests greater complexity in the structure of the thyroid gland. (Journal of Pathology and Bacteriology. 1923. pp. 459-469). According to these writers the unit of function is the lymphatic sinusoid (see diagram 1). The parenchyma of the lobule is divided by loose strands of connective tissue, in which mast-like cells are seen, into a series of well-defined functional areas or gland units. The fibro-elastic tissue forms a capsule which completely circumscribes each unit. Internally the capsule is lined by pavement endothelium. Both these layers are penetrated at two or three points by intralobular blood and lymphatic vessels. Each serous cavity is thus in fact a sinusoidal expansion of the lymphatic system. The epithelium of the gland unit appears in the sinusoidal space in long cylindrical columns which twist and turn in various planes to accomodate themselves to the

A.

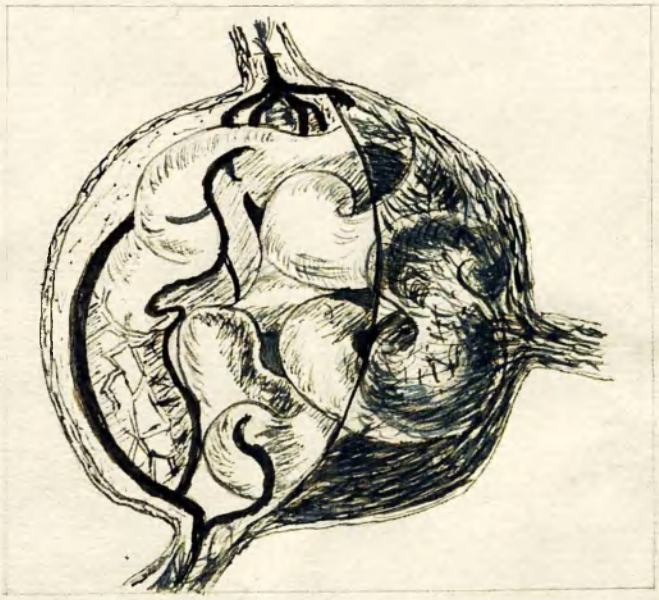
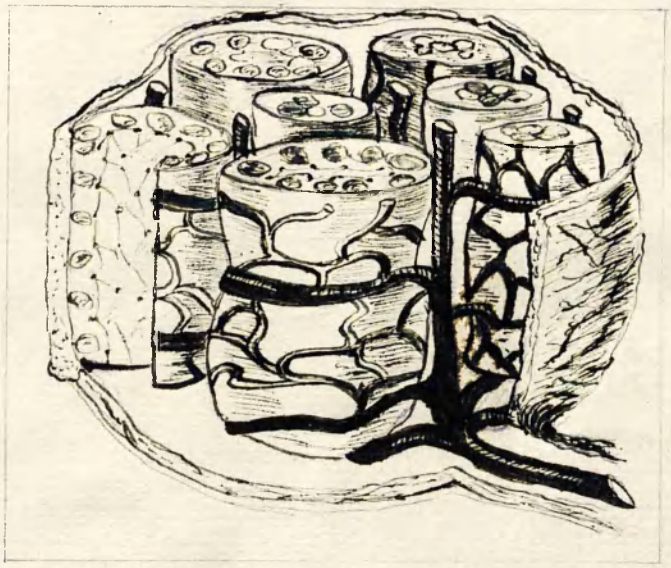


DIAGRAM. after Williamson & Pearse.

circumscribed area of the sinusoid. In all probability there is actually only one long convuluted column within each gland unit. Concomitant capillaries accompany the column in its various twists and communicating capillaries form a sort of basket work encircling the column. There is nothing but endothelium between the blood in the capillaries and the sinusoidal space.

According to Williamson there are two distinct cycles of function. One is the passive phase of vesiculation, whereby the excess or reserve of colloid is stored within the epithelial column. The other phase is that of active secretion in which a substance different in nature from the colloid is elaborated by the activity of the thyroid gland. (Lancet 1923, pt II, p. 1337). In the embryo and the new-born secretion seems to be the only product of the gland. After birth the colloid storage increases up to the age of five during which period secretory activity declines. From the age of nine to fifteen the secretory phase predominates and may completely overshadow colloid stage.

B.



apli Williamson & Pearse

From the age of eighteen to twenty years sex determines the picture. In the female the process is in the main a secretory one whilst in the male it is largely colloid. After this age the character of the female thyroid approximates to the male type except at the period of menstruation and during pregnancy (British Journal of Surgery, Vol. 13. 1926. Jan. pp. 475-487). A cross section of the normal gland shows the colloid in obvious vesicles collected into lobules bounded by a meagre interstitial tissue. There is little fluidity in the colloid so that the tissue cuts crisp, remains dry, and is very refractile. Storage of colloid by vesiculation predominates but opaque white streaks or patches can be seen representing areas where secretory activity is going on. Secretion stored by lacunation occurs alongside colloid storage by vesiculation. The storage of colloid is not essential for secretory activity, as is exemplified in the foetal and early infantile gland. When vesiculation begins in a unit a change takes place in the solid epithelial column. Colloid collects at discrete points in the column, and ultimately the column is fragmented into

into sections giving microscopically the appearance of vesicles. Between the vesicles cell masses can be seen, representing those places in the epithelial column that are not filled with fluid. It is the predominance of this cycle of function, says Williamson, which has obscured the essential morphology of the organ. Before a gland unit can take on a secretory function it seems that it must return to the indifferent solid phase. It cannot pass directly from colloid storage to secretory activity omitting the indifferent phase. In secretion the whole gland unit takes a part, the reverse of what happens in colloid storage where the whole function is limited to the epithelial column. The nuclear cytoplasm becomes laden with granules which ultimately liquefy and occupy the centre of the epithelial column, forming a lake. This is described as ~~lacimation~~ lacunation. The cells of the sinusoidal capillaries likewise become laden with granules, and lymphocytes appear in the sinusoid itself. Colloid seems to be a vehicle or carrier like the taurocholates and glycholates of the bile. As it is only

the excess of bile that is stored in the gall bladder so it is only the excess of colloid that is stored in the thyroid gland. These investigators have found that changes take place in the parathyroid glands that bear a definite relationship to variations in the thyroid phase. In secretory activity lymphocytes overflow from the gland units into the parathyroids through lymphatic channels that connect the glands together.. With the thymus gland an association is also observed. Increase in secretory activity in the thyroid gland is associated with increase in the number of lymphocytes in the thymus, whilst decrease in activity in the thyroid works "hand in glove" with fat accumulation in the thymus at the expense of the lymphocytes. When fluid secretion collects in the thyroid sinusoids it passes by lymph channels to the thymus. It would seem that these three organs - the thyroid, the thymus, and the parathyroid - work in combination. The thyroid is the main organ; the parathyroids act as sentinels to measure the efficiency of the thyroid glands, and through the sympathetic system adjust their

operations to the needs of the body, whilst the thymus is the reservoir where lymphocytes or fat are stored according to the phase in prominence at the time.

Our first discoveries of the function of the thyroid gland are the result of the early surgical work of men like Kocher. The theories of the earlier investigators were marked more by imagination than fact. Wharton associated the function with the contour of the neck. Boerhaave and Martyn thought it had something to do with voice production. In 1840 Sir Astley Cooper noticed the peculiar symptom complex after thyroidectomy. In 1889 Schiff called attention to the danger of thyroid insufficiency. Kocher in 1883 described the "cachexia strumipriva," which follows total extirpation of the thyroid glands. Reverdin was the first to give a full account of this cachexia in man. (Horsley. B.M.J. 1892 pt i. pp. 265-269). Gull in 1874 had described Myxoedema (Trans. Clin. Soc. VII. 1874) The similarity of the symptoms of cachexia strimipriva to idiopathic myxoedema was soon observed and

so the term "operative myxoedema" arose.

Hofmeister (Hofmeister F. Experimentelle Untersuchungen uber die Folgen des Schilddrüsenverlustes. Beitr z klin. Chir t 11 p 2, 1894) and von Eiselsberg (von Eiselsberg. Die Krankheiten der Schieddrüse. D. Chir. Lief 38 Enke. Stuttgard 1901) excised the thyroid gland soon after birth producing artificial cretinism. They found characteristic changes in the epiphyses of the long bones, changes which led Eherth to speak of "foetal rickets". (Phys. and Path. of Thyroid Gland Horsley 1896 pt ii p. 1623). The functions of the thyroid gland are somewhat complex. At least four different functions are known. The thyroid gland has a morphogenetic function in which it is associated in action with the pituitary, the thymus, the testicles, and the suprarenal glands. Inadequacy, as in athyroidism or hypothyroidism, interferes with the proper development of the tissues. The dwarfed form of the cretin is rarely if ever due to goitre in the child. The essential factor is goitre in the mother, although it is a fact that 75% of all cretins

are goitrous. In enthyroidism where the various functions of the gland are in a state of equilibrium growth takes place, that is to say, the function of the thyroid gland is anabolic . It has, however, another function which is distinctly katabolic. In this character the thyroid increases oxidation. "It makes the tissues as it were more inflammable so that they burn away more rapidly.", as Robert Hutchinson says. A third function attributed to the thyroid gland is the neutralization of the toxic products of normal metabolism. This was recognised as early as 1894 by Edward T. Blake in his"Account of Myxoedema, Cretinism and the Goitres". In 1912 Kocher observed the presence of methyl guanidin in the urine of parathyroidectomised dogs. Noel Paton found that thyro-parathyroidectomy increased the quantity of methyl guanidin in the blood. (T.B. Robertson Principles of Biochemistry p. 436). As the result of extensive experimental work Noel Paton and his associates concluded (Quart. Journ. Exp. Physiology 1916 pp. 203-382) that it is the parathyroids that control the metabolism of guanidin in the body and by

doing so they exercise a control on muscle tone. They also state that the parathyroids are implicated in idiopathic tetany. This question has importance in relationship to McCarrison's nervous cretinism. De Quervain considers this condition a combination of thyroid and parathyroid inadequacy or in other words a combination of ordinary cretinism with the clinical pictures of diplegia and tetany. (Goitre F. de Q. p. 188). Gley in 1913 (Arch. d. Physiol. 1913) considered the thyroid and parathyroid glands one in action. Vincent and Jolly do not admit a specific function to the parathyroids (Journ. Physiol. 1904 XXXII, 65-86; 1906 XXXIV, 295-305) although they accept the fact of their distinction embryologically. Sir James Berry too (Surgery of the Thyroid Gland. Brit. Med. Journ. 1913 Pt. I. pp.583-591) states that in operative work, provided one leaves the patient with a sufficiency of healthy thyroid tissue it does not matter whether the portion remaining includes the parathyroids or not. Never has he seen tetany in any of his cases, and only twice a transitory myxoedema.

Sir Victor Horsley (Brit. Med. Journ. 1892 pt I pp 265-268), found that thyroidectomy in birds never produced cachexia, in ruminants a slow developing cachexia, moderately rapid in man, and severe in the carnivora. Symptoms of muscular tremor and motor paralysis were seen in his monkey experiments, but he failed to distinguish between the thyroid and the parathyroid glands. In this connection the experiments of Halstead appear conclusive. He removed the four parathyroid glands and transplanted one of them in the abdominal cavity, and the result was that no symptoms appeared. When later this transplanted gland was removed symptoms of tetany appeared and the animal died. It seems clear then that tetany is a reaction to an acute intoxication, and that parathyroid secretion has the power of neutralising the toxic products of normal metabolism, but whether the thyroid gland also has the neutralizing function, which Moebius maintains, seems far from certain.

A fourth function attributed to the thyroid gland is that of defence against bacterial invasion. In 1902 Sajous

found that the injection of bacterial toxins into man or animal excited the activity of the thyroid gland. By injecting diphtheria toxin into guinea pigs Farrant produced thyroid hyperplasia, and he demonstrated that the effect of the toxin could be mitigated by injecting thyroid extract along with the toxin. Fassin found that thyroidectomy diminished the germicidal power of the blood. Vincent and Tolly observed how readily thyroidectomised animals succumbed to infectious disease. Gley found that thyroidectomised animals' blood serum was more toxic than the serum of normal blood so it would appear that there is ample evidence in support of the belief in the antitoxic and bactericidal power of the thyroid secretion (McCarrison. Etiology of Endemic Goitre).

This multiplicity of function is supported by the results achieved in the field of bio-chemistry. Sixty to seventy years ago Chatin held that goitre and cretinism could be prevented by the administration of small doses of iodine. Kocher at a later date observed the beneficial effects of

iodine in cachexia thyreopriva, and in 1895 he suggested the presence of iodine in the thyroid gland (Correspond. f. schwiz. Ärzte. 1895 XXV 3-20). Baumann (Zeitschriph f. physiolog Chem. Strasburg 1895 XXI. 319-330) showed that both the thyroid of man and animals contained appreciable quantities of iodine. Since that time many of the investigators have made complete analyses of the chemical constitution of the thyroid gland. Ordtmann found 81.24% of water, 17.66% organic and 0.1% inorganic matter mostly iodine. Roos found sulphur, nitrogen, carbon and hydrogen present in the gland and stated the percentage of each element. Others have found arsenic, fluorine, sodium, potassium, bromine, magnesium, calcium and silicon. It has been found that whilst many of the tissues of man contain iodine, the thyroid contains ten times more iodine than any other organ in the body. This amount varies with age and sex and is more abundant in the female (Cameron. Journ. Biol. Chem. Baltimore 1914 XVIII, 335-380). On an average the adult thyroid gland contains about five milligrams of

iodine. Zunk found as much as 15 mgms, in the thyroids of war victims struck down suddenly when in excellent health. The amount of iodine has a seasonal variation being more abundant in the summer months. Fordyce (Edin. Med. Journ. 1912, IX 55-62) and Cameron and Carmichael (Journ. Biol. Chem. 1920 XLV 69-100) found that the iodine was chiefly present in the colloid. Different substances have been isolated. Baumann discovered Iodothyrine which contains 10% iodine. He considered this brown amorphous powder as the active principle of the thyroid gland. It is similar to Roos's thyroidin. Oswald (Arch. f. exper. Path. u. Pharm. Leipzig 1909 LX 115-130; 1910 LXIII 263-269) isolated Iodothyreoglobulin. It contains 0.15% iodine. Notkin found an albuminous substance in the gland which he called thyreoproteid. Asher described thyreoglandol which is a very active substance, and yet it contains no iodine. In 1914 Kendall isolated thyroxin (E.C. Kendall Journ. Amer. Med. Assoc. 1915 XLIV.2042). It exists in three forms. The keto form crystallizes in needles, is tasteless and odourless. The enol form exists in alkaline solutions; the open

ring form is got by adding sulphuric acid to an alkaline watery solution of thyroxin. The iodine content is 65%. The chemical formula (Stephenson T. "Thyroxin, its history, chemistry, and therapeutics. Prescriber, 1922 Oct. pp. 334-335) is $C_{11}H_{10}O_3NI_3$. It is extraordinarily potent producing effects in such doses as 0.001 gramme. (Chem. & Physiol. Properties of Int. Sec. E.C.Dodds and F.Dickens). It acts as a catalyst. By its presence the amino-acids produced by partial proteid metabolism are further reduced to CO_2, H_2O, and NH_4CO_3. The ammonium compound is finally converted into urea by parathyroid action (Endocrinology. Walter Timme 1924 pp 27-47). "Deaminization" says Kendall, "is the function of the thyroid gland". The chemical constitution of thyroxin has been further investigated by Harington (Constitution and Synthesis of Thyroxin. Biochem. Journ. 1927 XXI 169-181). He considers that thyroxine is amino acid tyrosin with two iodine atoms replacing two hydrogen atoms of the benzene ring. The chemical formula is $C_{15}H_{11}O_4NI_4$. Lyon and Redhead (Synthetic Thyroxin. Clini-

cal Tests Edin. Med. Journ. 1927. April 194-199) have tried the thyroxin that Harington has prepared synthetically and have found it efficient in two myxoedematous patients.

Cramer's work (Prescriber 1924 May p.185) suggests that the mother substance of thyroxin may be tryptophan as he found thyroid atrophy in rats which had been fed on a diet lacking this amino acid. However, Hopkins has shown (New Physiol. A. Rendle Short p.37) that both tyrosin and tryptophan are necessary for life. Chang-Hsi-Chun (Amer. Journ. Physiol. 1925 July 275.286) believes that tryptophan does not affect the thyroid gland directly but that it produces its effects indirectly by disturbing the nutrition. Abel and his associates have concluded (Amer. Journ. Phys. July 1925 pp 287-295) that tryptophan is essential to the normal functioning of the thyroid gland. Weir, however, (Amer. Journ. Med. Sc. 1925 June 860-865) could find no relationship between thyroxin content, the tryptophan content and the basal metabolic rate. That tryptophan affects growth is generally admitted and it is well known that inadequate

thyroid secretion will stunt the growth of the long bones as is seen in cretinism.

Crile says the function of the thyroid begins and ends with iodine. (The Thyroid Gland. Crile and His Assoc. p. 25). Swingle (Endocrine pt.2 1918 p. 283) also considers that the only function of the thyroid gland is as a reservoir for iodine, that iodine, in fact, is the thyroid hormone. Many, however, do not accept this view. It does not follow that because iodine is a physiologically active material it is therefore the hormone of the gland. The same argument might be applied to arsenic. Arsenic is a very active substance but although it is found in the thyroid gland there is no proof that it is the active hormone. Again Baumann has found iodine sometimes absent from the thyroid gland in children. Roos found no iodine in the thyroids of four puppies. On the other hand Aesbacher found (Mitt. Grenzg. Med.. Chir. 1905) that the biological activity of the thyroid gland varied with its iodine content. The amount of iodine is proportional to the amount of colloid in the gland, whereas the phosphorus content depends on

the amount of cell nuclei present. Iodine is certainly an essential constituent of thyroxin. The highest iodine content is present in normal glands. In 1916 Marine determined that the thyroid cells had a special affinity for iodine. Crotti says there is an iodine function presiding over general metabolism, a phosphorus function regulating thermogenesis and vaso motor action, a sulphur function that controls skin nutrition, and an arsenic function active in connection with the nervous system. The pathology of the various forms of goitre have been studied by Marime and Lenhart. (Bulletin of John Hopkins Hosp. May 1909 Vol.20 No.218 pp.131-139). They concluded that excepting atrophies, neoplasms, and infections, all thyroids fall into four classes:- (1) Normal thyroids (2) Colloid goitres (3) hyperplastic goitres and (4) Complicated goitres. They consider that terms such as cystic, calcareous, fibrous, vascular, gelatinous etc. should not be included in a pathological classification, as they only indicate secondary change, and as Virchow has pointed out (Virchow, Die Krankhefter Geschwuls III 4) are of no primary significance. They experimented on

about 700 dogs, first removing one thyroid lobe, then after periods varying from seven days to a year the remaining lobe was excised in part and examined. In this way they were able to see thyroids in all degrees of change from the normal. They describe an early or preclinical stage in which, although clinically nothing can be seen, a definite change has nevertheless taken place in the thyroid gland. There is first of all (McCarrsion Etiology of Endemic Goitre) an increased blood supply to the gland, the capillaries are dilated, colloid is more liquid, and therefore stains more lightly. The cells lining the vesicles increase in size and may be cubical or highly columnar. The cells are more closely packed together and plications and papillation may be found. The gland has not yet enlarged in size. At a later stage the epithelial lining of the vesicles desquamates forming with the colloid casts in the vesicles. This irritation causes increased secretion and increased proliferation and consequently the colloid pressure inside the vesicle is increased causing

the vesicle to increase in size and the lining cells to become cubical or pavemented transforming the gland into the typical colloid goitre. Marine and Lenhart consider the colloid stage a reversion condition. They say colloid goitres are in all their anatomical characteristics the nearest approach to the normal gland. Their iodine contents are the closest in amount to those of normal glands that it is possible for glands that have once been the seat of active hyperplasia to assume. They state that on administration of iodine hyperplastic glands revert to the colloid type and in fact "they obey all the laws of normal glands in their anatomical, general, and biological characteristics". During the years of her married life a woman may show thyroid changes at each pregnancy, changes of hypertrophy and hyperplasia with reversion to the colloid state after parturition, but each return to the colloid state may be more and more limited, and so by a step-stair-like progress a chronic colloid goitre of considerable dimensions may be developed, and, as Allen Graham points

out, (The Thyroid Gland. Crile etc. pp.35-48) a more or less destruction of epithelium and secondary fibrotic change may occur marked clinically by the development of myxoedema.

Louis B. Wilson, director of Laboratories at the Mayo CIinic, Rochester, after a careful survey of 2356 simple and 1208 exophthalmic goitres removed at the Mayo Clinic stated that practically all cases of true exophthalmic goitre showed marked primary hypertrophy and hyperplasia of the gland parenchyma, whereas less than one per cent of the simple and toxic non-exophthalmic goitres showed any considerable degree of either hypertrophy or hyperplasia. Of the toxic non-exophthalmic goitres 50% were encapsulated adenomas, and the others showed chiefly a secondary regeneration of atrophic parenchyma. These secondary regenerations are usually recent enlargements of old colloid goitres. Of the simple goitre about half of these he found to be typical colloid goitres and the others mostly encapsulated adenomas.

In 1925 G. Scott Williamson and Innes H. Pearse built

up a pathological classification based on their anatomical and physiological investigations. They divided goitres into four classes:- (1) Hypertrophic (2) Hetero-trophic (3) Hyperplastic and (4) Heteroplastic. (Journal of Path. and Bact. 1925 pp. 361-387).

I. Hypertrophic Goitre.

By hypertrophy is meant nothing but an exaggeration of all the normal features of the various cycles of functional activity. This implies an increase in size and bulk but no hyperplasia. Whatever plastic changes take place are no more than what take place in the normal gland to make up for "wear and tear". In the normal adult gland colloid storage is the feature that predominates, but in the hyper-trophic gland secretory activity is the outstanding feature. On section, macroscopically, the gland is of a golden yellow colour, the interstitial stroma stands out and the secretory tissue may appear here and there as ischaemic nodules. The hypertrophy may be physiological, as is often seen in young girls at the time of puberty, or in older females associated with pregnancy. In status lymphaticus the hypertrophy is

pathological. One form of endemic goitre is the chronic hypertrophic gland. As a result of secondary fibrotic change in the hypertrophied gland dysthyroidism may be set up producing ultimately secondary Graves disease.

2. In Heterotrophic Goitre there is implied a want of balance in the relations of the two functional cycles of secretion and colloid storage. The goitre may be all secretory in type to the complete exclusion of colloid storage or it may be all colloid storage and no secretory activity recognisable. Heterotrophic goitre occurs in two varieties, depending on whether secretion or colloid storage predominates. It may be either Vesicular goitre or adenoid goitre and each of these may be found in the progressive or retrogressive stage.

(a) In the progressive stage vesicular goitre is marked by vascular engorgement of the perilobar and perilobular vessels, whilst the intrasinusoidal basket vessels and concomitant vessels are thinned out. The epithelium is quiescent and stains faintly. On section the gland is red, the distended

vessels are quite obvious, and cysts are often present. Microscopically the field is filled with thin walled vesicles and there is no evidence of secretory activity. In the retrogressive stage fibrosis will form large cysts in which calcareous or haemorrhagic change may occur. This is the typical colloid goitre. It also represents one of the types of endemic goitre.

(b) Adenoid Goitre is always found in clinical association with primary Graves' disease. Secretory activity is at a maximum. There is an absence of colloid storage. It is much paler than the vesicular type, and instead of being sticky it is soapy. It has an ischaemic appearance. Clear yellow fluid collections are found at the centre of some of the lobules. The epithelial cells are often cylindrical and show considerable desquamation. They tend to form papillae. The vesicles are of medium size. They are more or less irregular, and colloid material is usually absent. In the retrogressive stage the appearance will depend on the degree of cellular exhaustion and atrophy, but it will be firm and

fleshy and the soapy feeling will have departed. Pathologically Graves' disease shows three distinct stages. There is first of all increase in secretory activity but absence of colloid. There are very few lymphocytes. A post mortem feature of importance in association with this condition is enlargement of the thymus, and as microscopically the thymus contains very few lymphocytes, it can be inferred that the thymus is not storing much of the profuse secretion. This vicious secretion brings on the thyrotoxic stage, marked clinically by exacerbation. Ultimately as the result of diffuse fibrosis of the walls of the lymphatic sinusoids, a condition of atrophy may ensue ending in spontaneous cure.

3. Hyperplastic Goitre. This is the third type. Hyperplasia is a balanced overgrowth. It approaches the condition of the neoplasm. There are two varieties, the simple hyperplastic goitre, and the lymph adenoid or myxoedematous goitre. In the simple hyperplastic gland the lobes are widely separated from one another. It is the seat of an encroaching fibrosis. It consists of several encapsulated adenomata of

of a golden yellow colour. It is similar to what Wilson figures as toxic adenoma. These hyperplastic goitres may show neoplastic or degenerative changes, cyst formation, or a diffuse fibrosis. Lymph adenoid goitre is known as ligneous thyroid. Microscopically it can be distinguished from adenoid goitre by the abundance of lymphocytes all over the field. In fact it may look like a granuloma. Macroscopically it can not be distinguished from adenoid goitre. It is a type that occurs in people over fifty years of age, and is associated clinically with myxoedematous symptoms. Ultimately the outline of the sinusoids is marked microscopically by a whorl of fibrosis.

4. The heteroplastic is the last of the four varieties. Its name implies an unbalanced overgrowth. It occurs in two forms, primary intralobular fibrosis, and primary perilobular fibrosis. The former is a gland unit affection whilst the latter is a coarse fibrosis of the interstitia. The intralobular goitre is sometimes spoken of as vascular goitre. It is a vascular fibrosis surrounding the indi-

vidual gland units and extending to the enclosing capsule making its removal difficult. A fibrosis of this variety may be part of a generalised arterio-capillary sclerosis in a case of congenital syphilis. It is analogous to primary interstitial nephritis. This type is sometimes spoken of as toxic goitre, forme fruste, thyrotoxicosis or toxic adenomatosis, as is described by Emil Goetsch (Endocrinology 1922 pp.59-72). "The alveolar epithelium here undergoes atrophy and regression, and the thyroid intoxication is due to overaction of the abundant interstitial tissue".

Primary perilobular fibrosis as a secondary change is extremely common. Retention cysts are common, and haemorrhages may occur. The cysts may be colloid, or a mixture of colloid and parenchymatous tissue. Such changes may occur in endemic goitre. A similar fibrosis occurs sometimes in association with foetal adenomata. These arise from the embryonic cell masses described by Wölffler. The normal parenchyma takes no part in their formation. They are most common at puberty and may ultimately develop into a large

colloid goitre or many remain about the size of a lemon consisting of some twenty or thirty small adenomata.

Two physiological phases have been described. In endemic goitre two pathological types have been described:- (1) a chronic hypertrophic type in which secretory activity is marked, and (2) chronic vesicular goitre in which colloid storage predominates. In children De Quervain describes two types of simple goitre corresponding closely with the two types described by Williamson and Pearse. He says that in children up to twelve years of age goitre is usually diffuse and of a microfollicular type. There is increase in the number of vesicles and a decrease in the volume of the vesicles. Between the ages of twelve and sixteen there may be a disappearance of colloid associated with hyperplasia in the cellular elements, resulting in a condition that microscopically looks like a case of Graves' disease. The cells lining the vesicles multiply rapidly, papillae are formed, and desquamation is considerable. The vesicles are empty and very irregular. This is the par-

enchymatous goitre - the goitre of puberty. But this is not the only type. As De Quervain says (Pathological Anatomy of Goitre p. 25 A Contribution to the Study of the Pathology.....) at puberty the microfollicular type may proceed to colloid increase. The vesicles increase in size and the cells are cubical or flattened out. As the age of twenty is approached the goitre in both types tends to become nodular, the parenchymatous variety being transformed into a mass of adenomata, and the diffuse colloid goitre into a mass of colloid nodules from a pea to a nut in size - the so-called pudding goitre.

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SECTION 5.

Signs, Symptoms, Diagnosis and Classification.

The thyroid gland is intimately connected with the larynx; hence the most important sign of a thyroid tumour is that it rises and falls with the larynx and trachea during deglutition (Index of Differential Diagnosis - H. French. p. 721). Whilst this is generally true, and a most important diagnostic feature, there are certain fallacies that may arise. A cyst of the subhyoidean region, for example, may present this sign. Tumours arising either from the larynx or trachea may simulate thyroid conditions. Malignant growths springing from the pharynx and oesophagus, may readily be mistaken for thyroid tumours.

Another rare condition that may confuse the diagnosis, as recorded by Wolfenden, (Journal of Laryngology, 1888, p. 99) is tracheal hernia. Sebaceous cysts can be readily distinguished by palpation. The rare occurrence of a dermoid cyst in this region has to be remembered. Some people have fat necks and a fold of fat can quite easily lead to a wrong diagnosis if dependence be placed on mere inspection.

A cyst of the thyreoglossal duct can usually be differentiated by the fact that its usual location is in the mid-line of the neck and higher than the usual goitre. A lipoma attached to the thyroid cartilage has been mistaken for an enlarged thyroid. (Berry, Dis. of Thyroid Gland. pp. 72-104) Enlarged cervical glands, as a rule, do not rise and fall with deglutition, but, where the enlarged glands are tubercular, adhesions may give attachment to the trachea and so a participation in tracheal movements is obtained. On the other hand adhesions may prevent a thyroid swelling from rising and falling with deglutition. Osler (Montreal Gen. Hosp. Rep. 1880. pt. 1. p. 340.) records a case of lympho-sarcoma of the deep cervical glands involving the thyroid and simulating goitre.

Goitres vary considerably in size. A slight temporary enlargement of the gland occurs in anaemia and in pregnant women, but it is not sufficiently great to be considered as a form of goitre. (G.R. Murray. Greens. Encyclop. Pt. XXlll. p. 18). Simple parenchymatous goitre is the commonest variety in young people. The endemic variety often begins in the same way and, in children, the hypertrophy is usually diffuse and free from nodules.

At this stage it is amenable to non-operative treatment, but when proper treatment is not given the great majority of cases may undergo changes ultimately requiring surgical interference. (I. Bram, Goiter. p. 47) In long standing cases secondary changes, such as multiple cystic degeneration and fibrosis may occur. Cystic goitre may reach a tremendous size, such as those figured by Bruns and Bilroth. Alibert, (Nosologie Naturelle, Paris, 1817, p 468) describes some peculiar forms of goitre. Cystic goitres may reach a tremendous size and become pendulous (Goitre. De Quervain, p. 65). The neck may be so distended that it is quite impossible to tell by palpation whether the condition is of thyroid origin or not. Large goitres occur sometimes in children but such is not the rule. The goitre of childhood is usually a small diffuse hypertrophy affecting the isthmus and both lobes, thus maintaining more or less the horse-shoe shape of the normal thyroid. Not infrequently the right lobe is more enlarged than the left. In some instances there is an enlargement of the right lobe only.

About six months ago I saw a hypertrophy of the thyroid confined to the left lobe, but this is the only case of this kind I have found after an examination of many thousands of young people.

In children between five and ten years of age, it is not unusual to find swelling of the thyroid gland limited to the isthmus. At puberty the hypertrophy is usually diffuse and feels homogeneous but in some it is somewhat granular. In this condition it may cause no inconvenience and may, in some instances, be looked on as a physiological reaction to an increased demand for thyroid secretion, coincident with the awakening of sexual life. In adults a goitre may be large and cause little or no inconvenience, but the liability to toxic adenoma is ever present. Again in its increasing growth, dyspnoea may arise from compression of the trachea. Sometimes a goitre passes beneath the sternum and exerts a constriction on the veins at the root of the neck, producing in severe cases, the characteristic "caput medusae" or coils of distended and tortuous veins. Even in children a certain amount of venous distension is found in the neck in the region of the thyroid. In one such case, as it was possible to pass the thumbs between the manubrium sterni and the swelling, the condition of the veins was obviously not due to intra-thoracic goitre. It is possible that the compression of the veins was due to an enlarged thymus.

Substernal or intra-thoracic goitre is usually found in older patients. They come complaining of hoarseness, dyspnoea, dysphagia, headache, vertigo, tinnitus, and insomnia. There may be signs of "mechanical goitre heart". The suprasternal notch is effaced. The voice is thick, gutteral and muffled. (Crotti. Thyroid Gland. p. 143) Phillips, (Thyroid Gland, Crile and Assoc. pp. 65-98) records a case of intra-thoracic goitre that arose from an accessory gland in the mediastinum. As Richardson says, (The Thyroid and Parathyroid Glands. p. 96) the diagnosis of goitre of the accessory glands is attended with great difficulty. When a goitre is very movable, it may be drawn into the superior mediastinum, where it may remain till expelled again by forced expiration. At times it is intra-thoracic whilst at other times it is in the neck. Such a condition is described as "diving" goitre, and is frequently associated with choking spells. It is most important in suspected intra-thoracic goitre that an X-ray examination be made. A goitre can be distinguished from an aneurysm by the pulsatile character of the latter. Fluoroscopic examination should be made and photographs taken for future reference.

Nichols points out that an angle can be made out between the aortic shadow and a substernal goitre which he considers of diagnostic help. (Crile and His Assoc. pp. 109-139) An enlarged thymus is usually situated lower than a thyroid swelling and is triangular in shape. In the adult an enlarged thymus is often associated with exophthalmic goitre. Glandular development in Hodgkin's disease may confuse the fluoroscopic picture, but a blood examination should clear up the diagnosis when there is doubt. Other conditions that require to be distinguished are malignant disease, osseous tumour of a rib in the thoracic region, and lung abscess. Pneumonia at the apex of the lung may give a dense shadow extending to the mediastinum.

In children an ~~abscess~~ absence of symptoms is the characteristic feature of some. The children often come for treatment on account of the swelling in the neck - and not because they feel ill. Still this is far from being usual. During the year 1926 I kept a record of the medical history of every child that came for treatment. In 25% of my cases there was a history of rheumatism. It is rather surprising how many of those under treatment for goitre complain of rheumatism. I know instances where thyroid extract has cured rheumatism in which the salicylates were of no avail. Sergent (Monde

med. July 1. 1925. xxxv. p. 537) advises thyroid extract in combination with sodium salicylate. As regards nutrition a number of the children were subnormal whilst others appeared in good health. Hirsute deficiency I found in 13% of those who were under treatment. It is remarkable how often the eyebrows are poorly developed, especially in their outer thirds. Alopecia and ichthyosis occur occasionally. Frequently I have to advise operation for enlarged tonsils and adenoids. In others I have found that no progress was made in the reduction of the goitre till dental caries was corrected. Vaso-motor disturbances, such as chilblains, were sometimes complained of. The above symptoms associated with slow pulse indicate the hypothyroid state which is fairly common in the goitre of childhood in this neighbourhood. Sometimes a very different type is met with such as J.J. a boy aged 14 - he is a quiet industrious boy with intelligent but rather bright eyes. He has a tendency to open his eyes very wide. There is no exophthalmos and Stellwag's sign is absent. He has a habit of twitching his eyelids repeatedly, although there is no evidence of eye disease. The palms of his hands are moist. The pulse-count is 140 per minute. The heart sounds are normal, AND there is a slight tremor noticed when the arms are stretched out and the fingers separated.

No bruit is audible over the goitre which is considerable in size and has a granular beefy feel about it. The teeth are good and quite regular. This is the type classed by Bram as "puberty hyperplasia"; the symptoms are those of a mild hyperthyroidism.

Murmurs over the thyroid gland are not usual in simple goitre. In many cases a factitious murmur can be produced by slight pressure. Inherent pulsation occurs in exophthalmic goitre and may lead to a diagnosis of aneurysm as Dalrymple (Journ. Morb. Anat. Lond. 1828. i. 43-47) and Raynaud (Bull. Soc. de Paris. 1859 XXXIV. 348-350) have recorded.

In children dyspnoea is not often the result of an enlarged thyroid. At the same time where surgical interference is required in the goitre of childhood, it is usually on account of dyspnoea. About a year ago a boy of 13 years of age was brought to me by his father. The complaint was that during sleep this boy had to be wakened up as he seemed on the point of suffocation. This was a nightly occurrence. On examination I found the nose and throat normal and there was no evidence of cardiac or lung trouble. The thyroid was moderately enlarged and seemed to be pressing inwards. After a period of treatment with

iodine the symptoms disappeared. I have noticed slight dyspnoea and cyanosis in certain of the goitrous children when they are suffering from a "cold". The usual cause of dyspnoea in goitre is pressure on the trachea. Sudden occurrence of dyspnoea may be due to sudden haemorrhage into the thyroid gland, oedema glottidis, rupture of a cyst or abscess into the air passages or it may come on as a result of pressure in thyroiditis. In parenchymatous goitre pressure is usually bilateral as Winslow pointed out (Observation sur un goitre voluminense comprisant la trachee artere. Bull del'Athenee de med. and Paris 1816). The trachea becomes scabbard shaped as can be seen in Kocher's drawings (Langenbeck Archiv. f. Kiln. Chiv. 1883. Vol. XXIX Plate XI). Pressure at different levels from opposite sides may give the trachea an S-shape, and may force it to twist on its own vertical axis. Rose of Zurich (Der Krofftod und Radicalem der Kropfe. Arch. f. kiln. Chiv. Vol. xxii) described changes in the wall of the trachea such as fatty degeneration, softening and atrophy. It is doubtful if such changes actually take place. What probably happened was that the bending of the trachea caused increased tension on one side of the trachea and diminished tension on the concave aspect, and so a false impression might be given as to the state of the tracheal wall.

Professor Bruns did not find these fatty changes.

Pressure of a thyroid swelling may damage one or both recurrent laryngeal nerves. This is more frequent in malignant than in simple goitre. It is one of the serious dangers that have to be faced in thyroidectomy. These paralyses may be partial or complete. In complete paralysis the voice is suddenly lost and becomes exceedingly hoarse. In partial paralysis there is very little alteration in the voice but the patient is unable to produce a clear resounding cough. Damage to the superior laryngeal nerve with resulting anaesthesia is not common. "In all progressive organic lesions of the centres and trunks of the motor laryngeal nerves the fibres supplying the abductors of the vocal cords become involved much earlier than do the adduction". (Simon. Quoted by J.D. Lithgow, Diseases of Nose, Throat and Ear. A.Logan Turner 1925). Pressure on the cervical sympathetic nerves is rare except in malignant disease. When it is present there may be contraction of the pupil and narrowing of the palpebral aperture.

Dysphagia is a complaint that is occasionally made. If severe it may suggest malignant disease of the oesophagus. Koch reports a case where the dysphagia was so severe that death took place from starvation (Ann. d'mal d'oreille et du larynx.Paris. 1881 VII p. 86).

The differentiation of goitre has not yet attained scientific precision. The various states of thyroid activity may be tabulated as follows:-

1. Euthyroidism, in which the organ is normally at work.
2. Athyroidism, which indicates complete abeyance of function.
3. Hypothyroidism, which infers a diminution of action.
4. Hyperthyroidism, which means an increased activity and
5. Dysthyroidism in reference to abnormal states of secretion of the thyroid gland.

Athyroidism may be congenital in which case it is spoken of as cretinism. If acquired as the result of disease it is described as Myxoedema. It may follow total thyroidectomy in which case it is described as cachexia strumipriva.

Infantilism, according to Richardson, (The Thyroid and Parathyroid Glands p.144) is a term applied when the thyroid function is partially or completely lost before puberty. Hastings Gilford (Diff. Diagnosis. H. French. pp. 188-190) includes under the term infantilism thyroid and pituitary deficiency conditions, ateleiosis and progeria. Cretinism is most common where the endemicity of goitre is high (McCarrison. Thyroid Gland p. 125). He finds 45% of cretins to be goitrous. The chief features of cretinism are perpetual infancy of body and mind. The body never attains maturity of growth; the neck is thick and the face large. The whole body is short and stunted. The older the patient, the more striking is the discrepancy between age and size (Murray Diseases of Thyroid Gland pt I. p. 91). The skin is dry and puffy, the hair coarse and scant, the limbs short and the abdomen prominent and the movements are slow. When asked a question they are slow to respond. I have seen the adult cretin doing simple household duties such as sweeping the floor. Mc Carrison

describes two types of cretinism occurring in India. (Thyroid Gland pp. 133-134). The so-called myxoedematous type is that already described. The other type he calls "nervous cretinism" (McCarrison Lancet 1908 pt.II. P.1278). It is a kind of idiocy associated, not with the ordinary stigmata of the cretin, but with cerebral spastic diplegia. Probably the nervous type is commoner in this country than is usually supposed. In 1913 Langmead (Proc. Royal Soc. Med. 1913) demonstrated one case of this type. Chagas (Nouvelle Iconographie de la Salpetrière 1913 XXVI I) drew attention to the fact that in infants suffering from epidemic thyroiditis symptoms of cerebral diplegia were not uncommon. F.G. Crookshank (Lancet 1917 pt 2 pp.604-605) stated that he had seen between 20 and 25 cases of nervous cretinism in England, although he was absent from this country for a considerable time during the period of the Great War. A disease that may easily be mistaken for cretinism is achondroplasia, one form of skeletal dwarfism. (I have enclosed a photograph I took about two years ago

Kitty Duffy. Age 7.

Achondroplasia. Note short arms and legs, relatively long body. Hand typically trident. Mentally backward.

Achondroplasia.

Helen Prince - Born 12.12.15. age 12.
Head circ. = 21". Overhanging forehead. Limbs short and podgy. Lordosis very marked in the lumbar region. The hands are distinctly trident. Height of child is 38". Mentally she is backward.

of a typical case of achondroplasia) * On first sight the condition might be mistaken for rickets from the tendency of the legs to be bowed. The proportions are of the dachshund pattern with short limbs and relatively long body. The head is large and round with bulging forehead. The bridge of the nose is depressed. The abdomen is prominent, and this is exaggerated by the tendency to lordosis. The trident hand is well exemplified in this photograph. Lordosis is very marked in one of my cases. (HALEN PRINCE)

"Myxoedema" is a term in use for a collection of symptoms due to loss of function of the thyroid gland occurring after fifteen years of age. (Murray. Diseases of Thyroid Gland pt. I. P.30.) The loss of function is the result of a slowly developing fibrosis. It is more frequent in women than in men. The onset is gradual and is marked by the characteristic solid oedema of the subcutaneous tissue. The face lines are lost and the lower eyelids are baggy. The skin is dry, rough, and cold. There is a pink flush in each

* Since writing this I have seen 3 more cases of Achondroplasia in Manchester. In one of these cases there was also evidence of the so-called "Pink Disease".

cheek but the rest of the face is sallow. The hair is thin and scanty, and in some cases the head is altogether bald. The nails are cracked and discoloured. These patients feel the cold of winter very much, and are much more comfortable in warm weather. Marked intellectual changes occur in severe cases. As a rule the temper is placid. Hallucinations are common, and in advanced cases insanity may follow. Myxoedema is really an extreme form of hypothyroidism.

In hyperthyroidism the metabolism is accelerated. The B.M.R. is high and there is diminished carbohydrate tolerance. There is a tendency to sweating, palpitation and tachycardia. The teeth are in good condition, well formed and regular. The hair is abundant fine and glossy. The hands are moist. Graves' disease or exophthalmic goitre is a disease marked by greatly increased metabolism and heightened excitability of the whole nervous system. Its cardinal symptoms are tachycardia, exophthalmos, tremor and enlargement of the thyroid gland occurring in subjects of an average age of 35 years (Plummer Amer. Journ. Med. Sc. 1913 pt. 790-796)

Sir Bernard Spilsbury (Sudden Death. Practitioner 1917 p. 132) said that exophthalmic goitre occupied an important position as a disease liable to cause sudden death owing to secondary disease of the heart muscle, "in fact, death may occur suddenly with no apparent cause". J. Strickland Goodall and L. Rogers have established that sustained thyrotoxicosis results in definite myocarditis (Lancet, March 5th 1927 pp.486-488). Fahr found chronic interstitial inflammation in the myocardium (Centralbl. f. allg. Path. u. path. Anat. 1916, 27,1.). Goodpasture found acute necrosis of the cardiac muscle (J.A.M.A. 1921, 76, 1545).

Classification.

In 1921 Williams (Williams. Classification of Goitre Amer. Journ. Med. Sc. Vol. 161.1921. page 225) classified goitres in the following way:- (1) Simple goitre (2) Toxic Goitre and (3) Exophthalmic goitre. Of toxic goitres toxic adenoma is the most important. The symptoms of toxic adenoma are the symptoms of hyperthyroidism occurring in patients between 35 years and 60 years of age. Symptoms begin to appear on an average 14 years after glandular enlargement.

Exophthalmos does not appear but nervousness , tremor and loss of strength may be severe. The principal pathologic change is secondary regeneration of atrophic parenchyma. When it is of a diffuse type Goetsch (Endocrinology 1922) describes it as diffuse adenomatosis. Plummer (Collected Papers of the Mayo Clinic 1925 pp.518-528) says adenoma and exophthalmic goitre may be present a long time without being recognised. He points out that adenoma, whilst the B.M.R. is not as high as in Graves' disease, maintains a more steady level than exophthalmic goitre does. The latter disease is subject to remissions and relapses alternating one with the other, but each relapse is usually worse than the preceding one. Exophthalmic goitre has to be differentiated from a number of other diseases, such as shell-shock, hysteria, neurasthenia, paroxysmal tachycardia, pulmonary tuberculosis, mania and diabetes mellitus. Apart from appreciable exophthalmos and thyroid enlargement there are certain features of great importance in differential diagnosis. Heart hurry of over 90 per minute continuous day and night and not influenced by digitalis is important

as pointing to Graves' disease. An increased appetitie with a steady fall in weight is significant. Another important feature is the relative immunity to cinchonism. Goetsch (E.N.York State Med. Journ. 1918 XVIII 259) has devised a test that depends on the fact that in hyperthyroidism there is a constitutional hypersensitiveness to adrenalin. The serum test was devised by Kottmann of Berne (Kottmann K. Schweiz Med. Wochensh. 1920 p 644) and it is based on the principles of colloid chemistry. It is said to be of value, although such conditions as malnutrition and hysteria sometimes yield a positive reaction. Basal metabolism tests are open to many errors. The Bram quinine test is simple and safe. The diminished tolerance to carbohydrates has led to the hyperglycaemia test but it does not seem very satisfactory for purposes of diagnosis.

Israel Bram classifies goitres into four clinical groups:- (1) Simple goitre (2) Toxic goitre (3) Malignant goitre and (4) Thyroiditis.

Malignant Goitre is usually a malignant change in a previously existing goitre. Early diagnosis is difficult. It

is a peculiar fact that the goitre of Graves' disease is practically immune to malignant change. A goitre of long standing suddenly begins to grow rapidly. It becomes more resistant to palpation and adherent to the overlying skin. It becomes tender to the touch and shooting pains are complained of. The mass gets harder, and the skin more swollen and infiltrated. Pressure symptoms appear soon and affections such as dyspnoea, aphonia and choking may follow.

Thyroiditis is inflammation of the thyroid gland. Acute thyroiditis is usually secondary to infection elsewhere or may occur during an acute infectious disease. Pain is felt in the region of the gland and chilliness is complained of. There is a rise in the temperature. Dyspnoea and dysphagia may appear and symptoms of Graves' disease may supervene. Suppuration is rare. Inflammation and suppuration may follow tapping, infection, incision or other thyroid operation. Chronic thyroiditis is represented by Syphilis and tuberculous infection. A Wassermann test is valuable in suspected venereal cases. Subjects of phthisis often have

enlarged thyroids. It is very doubtful, however, if primary tuberculosis of the thyroid gland ever occurs.

The Blood In Goitre.

Blood Changes of a fairly definite character occur in endemic goitre. The haemoglobin index is reduced. The number of the erythrocytes may be subnormal. The leucocyte count is low, the lymphocyte count is relatively high and the reduction of polymorphs is very considerable. Eosinophilia is present and may be very high. In exophthalmic goitre there is also a diminution of the polymorphs and an increase of the lymphocytes. Here also there may be eosinophilia. These blood changes are common to all intoxications of intestinal origim and are by no means specific to thyroid disorders. As McCarrison says (The Thyroid Gland p.104) the employment of the "blood picture test" in differentiating simple goitre from typical cases of Graves' disease is valueless.

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SECTION 6.

Treatment of Goitre.

1. Prophylaxis.

The importance of prophylactic measures is universally conceded. In 1924 McCarrison (B.M.J. June 7th 1924 pt I p. 989) emphasized the gravity of the physical and mental degeneration which result from congenital goitre and stated that as many as 5% of all goitrous mothers were likely to give birth to cretinous, imbecile, or otherwise defective children. In Switzerland, according to Goodfellow, (The Triumph of Iodine, The New Statesman 6.12.24) fifty thousand cretins are recognisable at sight and cretinoid idiots and deaf mutes fill the asylums. In 1921 Hotz of Basel spoke of the great need in his country of prophylactic measures and made a strong plea for governmental assistance. (Hotz. G. Schweiz. Med. Wehnschr. Basel. 1921.51.1153). In America Jackson recently stated (Jackson, Arnold S. Med. Journ. and Record. 1926 pp. 748-750), that cancer and tuberculosis combined affected only a small portion of the

population as compared with the millions of the population suffering from goitre. He also stated that the incidence of goitre, cretinism, and feeblemindedness was on the increase in the United States. In countries where the incidence is high the question of prophylaxis at once assumes a position of national importance.

A. Iodine.

The first instance of preventing goitre on a large scale was accidental, and in connection with the sheep-raising industry in Michigan. At a time when the sheep raising industry in Michigan seemed doomed (Marime and Lenhardt, C.H. Further Observations on the relation of Iodine to the Structure of the Thyroid Gland in Sheep, dog and Ox Archiv. Int. Med. 1909 iii 66) salt deposits were found in the neighbourhood of the Great Lakes. It was observed that sheep fed with this salt soon recovered from their goitre. Marime and Lenhart found that the iodine content of this salt was high. The following year after an investigation into the cause of so-called thyroid carci-

noma in brook trout at Shady Grove, Pennsylvania, Marime and his colleague (Journ. Exp. Med. 1910 XII 311) and XII 455) concluded that this disease could he prevented by adding iodine to the food or water. In the Akron schools, Ohio, an opportunity was given to try preventive treatment among school children. After a period of seven months Kimball reported (Crile and Associates. The Thyroid Gland. O.P. Kimball. The Prevention of Simple Goitre in Man.pp. 159-184) that amongst those taking prophylactic iodine no new case of goitre had occurred during the months under observation, and of those who had been found with goitre at the first examination one third of the smaller goitres had disappeared and another third had considerably improved. On the other hand, amongst those not taking iodine, 20% of those found normal at the first examination were now found to have definite goitres. Baillarger (Enquête sur le goitre et la crétinisme Bailliere, Paris.1873) had at an earlier date experimented on certain school children with iodine and although his results were most satisfactory he did not

continue the treatment. To-day prophylactic measures are established on a fairly sound basis.

In the prophylaxis of endemic goitre different methods have been employed. One of the most remarkable experiments is at present being carried out at Rochester, U.S.A. by which iodine in the form of sodium iodide is being artificially added to the water supply of that town twice yearly over a period of two or three weeks each time. The amount of added iodine is small and equals 16.6 lbs of sodium iodide to 25,000,000 (U.S.) gallons of water. There are certain difficulties in the application of iodine to water supplies. People drink very variable amounts of water and so very variable amounts of iodine are thus ingested. Again if the amount of iodine in the water is considerable adults especially those over 40 years of age, will be apt to develop hyperthyroid symptoms. On the other hand if too little iodine is added the amount may be insufficient to produce the desired effect. The economist may grumble at the waste of iodine since the larger portion of our water is used for other than drinking purposes. Again the "individualist" may

complain at the interference with his liberty, thinking, no doubt, that the iodine treatment should be limited to the actual sufferers. After all the scheme is not so much curative as preventive in intention. It is an effort to reach the possible sufferers, in other words, it is an attempt to prevent the development of goitre in those who would not escape otherwise. Since it is impossible to diagnose in the case of children and young adults which are and which are not destined to be affected the experiment aims at safeguarding the interest of the few by treating the whole water supply with iodine (Editorial "Indian and Eastern Druggist" p.68 March 1926). With regard to the danger of hyperthyroidism Hartsock of Cleveland raised a warning voice (Journ. Amer. Med. Assoc. May 1st 1926). Bram also raised objections to the wholesale use of iodine among adults (Archiv. of Pediatrics. June 1925 p.746). Boothby (Collected Papers of the Mayo Clinic and Mayo Foundation XVI 1924 pp 435-442 "Iodine in Prevention and Treatment of Goitre") thinks the arguments usually advanced miss the mark.

He says the "safety discussion" is so often centred round the amount of iodine given when the all-important factor is the presence or absence of adenomatous tissue in the persons subjected to the iodine. Generally adenoma is not found in children. The majority of workers consider iodine contra-indicated in adenoma but there are some who give iodine prior to operation in these cases. The older the patient and the larger the goitre the more likely is adenomatous tissue to be found. This explains why Boothby considers iodisation of the water supply a less satisfactory method of prophylaxis than giving iodine directly to school children only. Sir J. Houston (Medical Officer 24th Jan. 1925 p.41 "Medication of Water Supplies") says that as the dose is so very small the danger is insignificant.

In 1922 the "Swiss Goitre Commission" recommended the introduction of iodised salt for all (2.5 mg.iodine per kilo. salt) and tablets of iodostarin (1 mg iodine per tablet) for all school children. The dose of iodostarin is one tablet weekly for prophylaxis. Fellenberg estimated that the iodine

normally consumed with water and food at Chaux de Fonds, a district where goitre is rare, was on an average 11.4 mg. per annum whilst at Signau in the Emmenthal, where there is much goitre, the annual intake of iodine was 4.7 mgs. (Fellenberg Th. Biochemische Zeitschrift 1924). The annual consumption of table salt is about 2 kilos hence the intake of iodine from table salt according to the estimate of the commission would be about 5 mgs. of iodine per annum. The figure allowed is low but then allowance has to be made for iodine received from other sources. Iodised salt has been widely adopted in New Zealand, America, and the Austrian Tyrol. In this country Dr. Wheatby, M.O.H. Shropshire, has taken a leading part in the introduction of iodised salt in his own district (Kenneth Fraser, Deputy M.O.H. Cumberland "Iodine"). Since the introduction of iodised salt Bircher noticed an increase in the number of cases of toxic goitre at Auran. Plummer noted a similar increase in toxic cases at Mayo. In a paper read before the Swiss Goitre Commission (La Prophylaxis du Goitre Rev. Suisse d'Hyg. 1922) De Quervain urged that, as he had found the thyroid abnormally

large in the infant cadavers in the Swiss goitre centres and since he had found that fully 75% of all children entering school for the first time at Berne had appreciably enlarged thyroids, prophylaxis must begin before the school age. To be effectual he considered that treatment must begin with the mother and this he thought to be practicable only with iodised salt. Iodised salt as a general prophylactic is only intended to supplement the iodine we get elsewhere and so it is wise to keep the quantity low. However it is well to let it be widely known that some of the iodine preparations of salt on the market contain far too much iodine. It has been stated that iodised salt gives a much larger proportion of the toxic cases than iodostarin does. This may be due to the slower absorption of iodine in the stearin tablet form.

As has already been said iodostarin as a prophylactic in school children consists of a weekly dose of one to five milligrammes of iodine in the form of a chocolate pastille. In the centres of St. Gall, Berne, and Zurick such treatment has reduced the incidence of goitre from 75 to 27.5%.

Marine and Kimball in their experiments at Akron used sodium iodide. Bram prefers syrup ferri iodide. Hunziker and Wyss (Hunziker H. and Wyss M.V. Schweiz. Med. Wehnschr. Basel 1922. 52.49) tried one milligramme of potassium iodide weekly throughout the year. Iodised bitter scotch is a pleasant form. Fry of Bristol turns out iodised chocolates. Hunziker has suggested (Hunziker H. Cor. Bl. f. Schweiz. Aerzte Basel 1918. 48. 247) that the use of iodised manure in regions where goitre is endemic might enrich the vegetables of the district as regards their iodine content and as a consequence the disease might be eliminated from the neighbourhood. Fellenberg (Biochemische Zeitschrift. July 1925 pp.210-224) also reports the results of his work in connection with iodine. He found that feeding cows with beetroot leaves enriched with iodine yielded a small but appreciable increase in the iodine content of the milk. He suggests the possibility of being able to supply the necessary amount of iodine required by man in this natural way. Another method, suggested by Weith, (Weith. Abs.Journ. Amer. Med. Assoc. Nor. 1919.1561) is that which has been tried in Lausanne. Large

wide-mouthed bottles containing 20 grammes of 10% tincture of iodine are placed in the class rooms and allowed to escape into the air which is being constantly aspirated by the school children. The administration of iodine to school children may be criticised on account of the irregular manner in which the iodine is supplied and also on account of the large doses usually administered. Again there is the inadequacy of a scheme of prophylaxis to one section only of the population of a goitrous area. It can be said in favour of the Swiss method of adding iodine to salt that such a scheme is more comprehensive and more physiological. It has been shown both by Fellenberg and the New Zealand workers that the daily ingestion of iodine in the food supply of a non-goitrous area is 34.85 γ (that is, microgrammes of iodine per kilogramme food) whereas in a goitrous area the iodine intake is on an average about 20.15 γ. This gives a difference of 14.70 γ. Now the average daily consumption of salt from all sources is about 6 grammes. The addition of one part of potassium iodide to 250,000 parts salt gives a daily increased iodine supply of

24 γ and this is ample for the endemic areas so far investigated. Another point in favour of adding iodine to salt is the factor of economy. The use of iodine rich manures to enrich the soil or the giving of iodine to cows and fowls to enrich their produce is expensive. It has to be remembered too, that commercial salt is an unreliable source of iodine supply as often it is found to be iodine free. Whilst the amount of iodine advised by the Swiss Commission may be considered safe and although it is true that the normal thyroid gland can be subjected to large doses of iodine with no ill effects, as is evidenced in the treatment of syphilis with potassium iodide, it has to be recognised that the pathological gland, especially in later adult life, is highly sensitive to iodine. Fortunately the enlarged thyroid of the child and adolescent can tolerate doses of iodine much in excess of its requirements. In fact, Hotz in 1922 declared that the daily intake must reach 700 γ before any harmful effects on an enlarged thyroid need be anticipated. In Michigan where Hartsock found so much hyperthyroidism

following the use of iodised salt the fault lay in the excessive amount of iodine that was present in the iodised salt of Michigan, being in fact fifty times more concentrated than that used in the majority of endemic centres.

B. A simple means of prevention is the avoidance of endemic areas. Crotti describes how the pregnant women of Valais were wont to leave their homes during pregnancy and live for a lengthy period in non-endemic districts. In some cases the baby was left behind for some years in what was known to be a non-goitrous area (Crotti. The Thyroid and Thymus p.301).

C. The protection of water supplies is a factor of importance. It has been clearly demonstrated that the introduction of a pure water supply has been quickly followed by a reduction in the incidence of goitre in endemic areas. (McCarrison. Experiment in Goitre Prevention. B.M.J. Sat. Jan.15. 1927 pp.74.75). Ash attributes the reduction of the goitre incidence in Derbyshire to the purification and improvement in the water supplies in that county (Journ. of

State Medicine Nov. 1926 pp.627-640).

D. Diet is a factor of great importance. Even in districts where there is no deficiency in the soil iodine many cases of goitre of a sporadic type are found. Experience among the Jews has convinced me that diet is a most important factor. The diet of many of the poor children in this area is distressing. Often the parents are out working all day and a child of twelve to fourteen years is left in charge to attend school and look after her younger brothers and sisters. A dinner of white bread and tea is far from uncommon among our English working class children. They practically never get a substantial meal in the poverty stricken homes. Even among the children receiving free dinners because of extreme poverty I have noticed a disinclination to good vegetable soup whilst white bread is eaten with avidity. There is, I fear, a great deal of truth in Saleeby's statement (Iodine and National Health) "We do not know what we do in our seeming cleverness. We invent window glass which seems to let through all the light; we do not notice that the ultra-

violet is excluded to our detriment or destruction. We invent water purification systems excluding all manner of undesirable impurities and do not notice that we have also excluded the iodine without whichno man can live. We devise clever milling machinery and prepare beautifully polished rice or white flour and do not notice that the vitamines and iodine are missing". The importance of the vitamines has been well demonstrated by McCarrison in his most recent work on White Rats, in which he describes (Lancet April 30.1927.pp.916-920) a form of goitre histologically resembling the hyperplasia of Graves' disease and not due to iodine deficiency. He has also shown, in his experiments on pigeons, the importance of a well-balanced diet in the prevention of thyroid enlargement (B.M.J. 1925 June 13 1065-1069). Believing in the infective nature of goitre(McCarrison. The Thyroid Gland 1917 pp.104-105) he advises the protection of food from flies. He also thinks that care should be taken to prevent the handling of food by goitrous cooks and servants of dirty habits. He also

advises the boiling of drinking water, the improvement of personal hygiene, the abolition of cesspits and manure heaps in the proximity of dwelling houses.

Race.

Fukushima of the Royal University of Tokio in 1922 found that there was very little goitre among the Japanese. (J. Jap. Soc. Int. Med. 1921.9.No.5; Jap. Med. World.1922. 2.45.). He estimated that the iodine content of the thyroid gland in the adult Jap was much higher than the amount in the European thyroid. The immunity to goitre appears to be due to the inclusion in their diet of seaweed. (Seaweed contains 48,000 γ iodine as compared with .002 γ iodine in white bread. The Iodine Contents of Foods. Hercus and Roberts. Journal of Hygiene March 1927 pp.49-83 III B). The Japanese enjoy no hereditary immunity (W.O. Keith.Canadian Med. Assoc. Journ. Oct. 1926).

The Indians of the Pacific north-west were found free from goitre although this malady was quite common among the Europeans in the neighbourhood. (H.P. Rush and Jones, En-

docrinology 1925 Vol. 9 pp.372-382). The distinction was not in racial susceptibility for generally in North America Indians are as much affected as others. There is no doubt that the salmon of which these Indians on the Pacific had such an abundant supply and of which they ate so much supplied them with an abundance of iodine and protection from goitre.

In Graves disease, on the other hand, race plays an important role. Although the Jews as the result of their wise dietetic habits appear to be relatively free from simple goitre they are particularly prone to exophthalmic goitre owing to their high strung temperament. The Caucasians are considered the people most liable to affection whilst the phlegmatic negro is relatively immune. In this country Campbell (Geograph. Distribution of Goitre in School-Children in England and Wales. Journal of Hygiene March 1927 pp.1-18) believes that there is some correlation between goitre incidence and deaths from exophthalmic goitre but this is far from clear.

Strain.

This is another factor of importance in prophylaxis. It

is noteworthy that many of the goitres seen come on first about the period of puberty. This is especially true with regard to the female sex. There is a very definite relationship between the gonads and the thyroid apparatus. Physical and mental repose during the menstrual period would do much, Bram thinks, to lessen the incidence of sporadic simple goitre in young females.

Selinger (New York Med. Journ. and Med. Record April 4th 1923) thinks that the increase of goitre in the United States observed among adolescents is probably due to the fact that a large number of the female population of this generation are engaged in business. Greater energy demands are made and this necessitates increased metabolism. More iodine is needed and if not forthcoming thyroid enlargement takes place. Factory life in these competitive days is especially productive of fatigue and consequently anaemia, with a resultant intestinal toxaemia and thyroid enlargement.

Drug Treatment.

A. Iodine.

Burnt sponges have been used in the treatment of goitre

from the earliest times. Roger of Salerno observed the value of seaweed but it was not till 1820 that it became known that the value of this treatment was dependent on the iodine present in the seaweed. In this year Coindet, a Swiss physician, discovered the beneficial effects of iodine in the treatment of goitre. In 1850 Chatin maintained that goitre and cretinism could be prevented by the administration of small doses of iodine. He found iodine present in water cress and other plants which were in use against scrofula, tuberculosis, and endemic goitre. (Researches on the Occurrence of Iodine in Nature. Thos. V. Fellenberg 1924). So well known did iodine become in the treatment of goitre that in some endemic areas, as St. Lager tells us, many of the inhabitants were wont to carry small flasks of iodine around their necks from which they refreshed themselves from time to time. To-day both in prophylactic and curative treatment iodine is the most used of all known remedies.

In the treatment of <u>simple goitre</u> McCarrison considers

iodine the most potent remedy we have (The Thyroid Gland 1917 p.107). Marime and Kimball have said that so long as the iodine store in the thyroid gland is maintained above 0.1% no hyperplasia can take place. (Journ. Amer. Med. Assoc. 1921. 77.1068). The same preparations of iodine are used in the treatment of simple goitre as have already been discussed under prophylaxis. A useful adjunct to the administration of iodine internally is the external application of an iodine ointment. Employed alone, ointment is of little service but when combined with other more substantial measures it seems to expedite results. For psychological reasons Crotti (The Thyroid and Thymus Glands p.307) advises that the thyroid region should be gently rubbed with an iodine ointment for a period of five to ten minutes daily.

In exophthalmic goitre also iodine is sometimes employed. In 1803 Trousseau accidentally prescribed iodine instead of digitalis to a patient with Graves' disease. When he discovered his mistake he hastened off to see the lady expecting to find her much worse. Greatly to his surprise he found her

much better for the iodine treatment. In 1923 Plummer made a convincing report on the value of iodine in Graves' disease. In 1924 Plummer and Boothby (Iodine in Exophthalmic Goitre. Collected Papers of the Mayo Clinic and Foundation 1924 pp.421-424) reported that in 1200 cases of exophthalmic goitre they had seen no patient made worse but many improved after treatment with Lugol's solution. In the Mayo clinic prior to this date there was an average loss annually of fifteen patients with Graves' disease prior to operation. In the nine months following the use of iodine only four deaths occurred. They tell of the moribund patient with persistent vomiting and intestinal crisis brought round and in a state of repose in 24 hours as the result of iodine treatment, an effect as startling as that which insulin can produce in diabetic coma. However, it has to be remembered that the prolonged use of iodine does not cure Graves' disease (Collected Papers of the Mayo Clinic and Foundation XVI 1924 pp.434-442 N. Boothby "Iodine in Prevention and Treatment of Goitre").

In thyroid adenoma it is generally held that iodine treatment is unsuitable. However, there are those who use iodine in adenoma and adenomatosis. In fact Graham considers

that exophthalmic goitre and adenoma are clinical varieties of a single disease and that the reaction to iodine is the same in both. (Exophthalmic Goitre and Toxic Adenoma. Journ. A.M.A. 1926 Aug. 28 pp.628-631).

"On the Iodine Question" Kimball gave some valuable information in 1925. (O.P. Kimball. Induced Hyperthyroidism. Journ. A.M.A. Nov. 28, 1925 pp.1709-1710). During four and a half years he treated 2659 cases of hyperthyroidism; 309 showed signs of having had the symptoms precipitated or aggravated by iodine. Of these 309 cases, there were 210 in which the goitres had been of long standing and contained adenomata. Six patients with nodular goitre had been taking iodised salt; thirty-seven had used sodium iodide and the remaining two hundred and sixty six had been taking iodine under medical men as sodium iodide, Lugol's solution, or as syrup ferri iodidi. He concluded that the dosage of iodine should be reckoned in milligrammes; the maximum for the adult should be 10 mgms. (which equals $\frac{1}{6}$ of a grain) daily for not over one month during which time the patient is under close observation. One tablet of iodostarin (which is equal to 5 mgs or $\frac{1}{12}$ grain)

he considers may be given daily throughout alternate months without causing toxic symptoms but even here caution must be used. He believes that long standing goitres should be treated surgically if hyperthyroidism is present but that the goitres of young adults and adolescents should first be tried under drugs but even here iodine should be thought of in terms of milligrammes. He states definitely that there is no danger in the routine prophylaxis in school children by the weekly administration of 10 mgs of iodine.

B. Thyroid Extract.

Bram believes (Goitre .84) that whilst iodine is advantageous in endemic goitre thyroid extract and not iodine serves the purpose in sporadic cases. In puberty hyperplasia it does not seem to me that either iodine or the dried thyroid substance ~~are~~ is advisable. In these children tachycardia is very easily induced, apart from other symptoms and signs of Jodbasedow (Ueber Jodbasedow Arch. f.klin. chir. Berlin 1910 XXII 1166 Th. Kocher). Tachycardia due to thyroid extract has, however, to be distinguished from rapid heart action due to other causes. An emotional nervous temperament

is enough to produce frequency of the heart's action in young people. Again paroxysmal tachycardia and auricular fibrillation have to be kept in view before the thyroid substance is blamed. The onset of sore throat and influenza are frequently associated with a rapid pulse even before the temperature rises.

In cases of obesity thyroid extract must be used with great care as cardiac degeneration has to be suspected in these patients. The use of corpus luteum and pancreation have proved of service in some cases with tachycardia. Whilst in some respects corpus luteum is antagonistic to thyroid substance it may have a synergistic action by relieving pelvic dysfunction.

The cutaneous eruptions, articular and muscular pains reported by some as a result of thyroid extract, I have never seen. These symptoms are probably to be referred to the introduction into the organism of an albuminous substance of of animal origin. As the result of his experience in the treatment of 350 cases of goitre Kitchen (Canad. Med. Assoc. Journ. Aug. 1926) concluded that dessicated thyroid in small

doses gave a greater number of good results than iodine did. He found that doses of one to two grains to children daily produced no untoward effect even when given continuously for several months.

C. Treatment of Focal Infections.

These infections require to be sought out and treated (1) Chronic disease in the ear, nose or nasopharynx may cause an enlargement of the thyroid to continue in spite of the administration of iodine or thyroid extract. With regard to the tonsils Bram (Med. Journ. and Record.April 6th, 1927 pp.442-445) says that it is doubtful whether or not diseased tonsils play an etiological role in simple goitre. He considers however that in Graves' disease, diseased tonsils act as a contributory factor in the etiology. Still he thinks diseased tonsils should be removed even though the results are not very striking as far as the thyroid swelling is concerned. De Quervain (Goitre p.92) gives a warning against going too far in the investigation and treatment of focal infections. He refers to a young girl who was slightly hyperthyroidic and died after her sixth focal operation because

the surgeon's curette entered the meninges during the curetting of a real or supposed ethmoidal sinusitis.

(2) For intestinal disinfection McCarrison advised the use of thymol in 10 grain doses night and morning as a powder and taken with a glass of water. He gives warning about the solvent action of fats, oils, alcohol and vinegar. Mc Carrison got good results with soured milk prepared from the bacillus Bulgaricus. Messerli has also contributed to this method of treatment, but the question is still open. (Messerli F. Contribution a l'étude de l'étiologie du goitre endemique. Le traitement du goitre par la disinfection intestinale continue au benzonaphthol. Rev. Méd. de la Suisse romande p.4.1918).

(3) Vaccines prepared from intestinal organisms have been tried. They were successful in curing goitre of recent origin when injected at weekly intervals in appropriate doses.

D. Treatment at the Clinic M.E.C.

During the years 1925 and 1926 treatment for simple goitre was given at one of our school clinics. Apart from children who were already under treatment at the beginning

of 1926 a total of 154 boys and girls were admitted for treatment during the school year. This number was made up of 15 boys and 139 girls between the ages of five and fourteen years.

On the first visit to the clinic a complete examination of the young patient is made. The rate, rhythm and condition of the heart is noted. Enquiry is made concerning previous illnesses. The family history is investigated especially as regards presence or absence of thyroid swelling. An entry is made of the state of nutrition, of the condition of the skin and the hair. The gums and teeth are examined and the nasopharynx is investigated. Enlarged tonsils and adenoids are attended to at our special clinic for these cases. Other focal infections are referred to their appropriate departments. Where the nutrition is much below average we try to get the patient to one of the residential schools in connection with the Education Department of Manchester.

Altogether 93 children were treated with iodine internally and externally. For internal use chocolate iodostarin

tablets prepared by Hoffmann La Roche were employed. Each tablet contains the equivalent of five mgms iodine and is similar to what is used in the endemic areas in Switzerland. It was very seldom we had any complaint about the taking of these tablets. Some doctors have reported iodine rashes in their cases but this has not been my experience here. During treatment one girl of eleven years developed styes. Refraction of the eyes was done and proved that glasses were not required as both eyes were emmetropic. Focal treatment was given for the eyes but the styes continued to appear till the iodine was stopped. After this the eyes were soon well. Iodine was again tried but had to be abandoned altogether. The goitre although small was nodular and responded badly to every remedy that was employed. In 1923 F. Parkes Weber reported cases of iodism with facial oedema which responded quickly to adrenalin (British Journ. Derm. and Syph. 1923 XXXV.169.180). Snell and Sarim (Lancet April 9th 1927 p.789) reported a case of idiosyncrasy to iodine that resulted in oedema glottidis of such severity as to necessitate tracheotomy.

For external application iodex ointment has given most satisfaction. Other preparations of iodine have been tried

but they proved too irritant and were discontinued.

The children attended the clinic at least once a week. Of the 93 cases taking iodostarin (10 mgs weekly) internally. and iodex (externally) 42 were cured and 29 much improved. In some cases the thyroid enlargement disappeared in a few weeks. In the remaining 22 cases the iodine produced no reduction in the size of the gland. The diffuse soft goitres responded quickly and well but the small hard goitres that had been present from infancy did not do well under iodine. Cystic goitre did not respond to iodine treatment at all. A very noticeable feature in iodine treatment is the general improvement that takes place in the general health of some of these children. When they come here for treatment on account of goitre it has been noticed how poorly nourished, puny and pale many of them are. After a course of iodine they seem to blossom out, improve in appetite, in colour, and in vigour even though the goitre itself in some cases shows no improvement. So marked has this been in some cases that it has been felt that the goitre after all was only an

indication of the iodine deficiency.

Sometimes where iodine failed thyroid substance has proved useful. Treatment is usually begun with ¼ grain of the dry extract every other day for a week or two. After this, if there is no contra-indication, the dose is increased to ¼ grain daily for a fortnight. Every fourth or fifth week the extract is stopped for a week to avoid cumulative action. Gradually the dose is raised to ½ grain daily. Larger doses than this (in children under 14 years of age) are not required in the majority of these hypothyroid cases. Occasionally the extract has had to be stopped on account of tachycardia with tremor. Rarely faintness is complained of. In one case excitability and restlessness were induced. On another occasion sleeplessness occurred but it was uncertain whether or not this was due to the treatment. With regard to thyroid substance it is important to order it in small quantities as when it is old it is quite useless. Bram (Goitre p.85) says that when kept it may go bad and produce ptomaine poisoning. Some individuals are extremely sensitive to dried thyroid. One

young lady said it made her feel very "jumpy" and she certainly looked it although she seemed to be benefited by the treatment. It certainly reduced her excessive fat.

Manganese and thyroid substance have been tried and have proved successful in recent cases. Kaolin also has been found useful and emulsion of the bacillus lacticus has been on trial for some time and seems helpful in cases where neither iodine nor thyroid substance are suitable.

During the year 1926 a special lamp for radiant heat has been in use (200 V.200 W). The child is seated before the lamp and the neck is made bare. The lamp plays on the thyroid area for five minutes at a distance of eighteen inches. The eyes are carefully bandaged to prevent any damage to them. After five minutes' exposure iodex ointment is applied as a dressing to the neck and a further exposure for fifteen minutes is given. At the end of that time much of the iodex is found to have been absorbed. This treatment is repeated daily till satisfactory improvement is obtained. There is no doubt that good results have been obtained this way in parenchymatous goitre. In cystic goitre no cure was

obtained nor even improvement. Screening with ruby, violet and amber shades has been tried but the results have not been convincing. With the lamp treatment in girls about the age of puberty I sometimes combine pluriglandular therapy and for this purpose hormotone has proved useful. It is worth mentioning that in one case where treatment had been stopped owing to the girl reaching the age limit for school attendance and although the goitre was somewhat improved but not cured, on examination some months later the enlargement was completely gone and the girl felt perfectly well. This seems to indicate that light treatment should be stopped short of complete cure lest over treatment might possibly induce myxoedema to a greater or less degree.

X-Rays and Radium.

X-Rays. In simple goitre medicinal methods of treatment are usually more applicable than radiation. One difficulty in X-Ray treatment is the impossibility of telling to what extent the normal as well as the diseased tissue is destroyed. Again simple thyroid enlargement is generally

compensatory in character hence the destructive effect of X-Rays may lead to myxoedema. The danger of causing peri-thyroid adhesions is perhaps the most serious drawback to this method of treatment.

In exophthalmic goitre there are many who claim good results following X-ray treatment. W.H. McGuffin (Canad. Med. Assoc. Journ. Oct. 1926 pp.1182-1187) treats the milder ambulatory cases with X-rays but the more severe cases he confines to bed and treats with radium. One great advantage in X-ray treatment is that there need be no serious interference with the patient's occupation. This is an important matter to a married man with a family dependent on his income. McGuffin gives five minutes exposure to each side of the neck once weekly for a period of four weeks. After this he allows a fortnight's freedom from treatment. Then four subsequent exposures are given at weekly intervals. He may give further exposures at fortnightly intervals if he considers the basal metabolic rate so demands. He finds that it is seldom that his patients get nauseated although

they may complain of warmth and swelling of the tissues of the neck. This condition however is transient, passing off in a few days at the latest. In the very toxic cases there is sometimes a slight increase in the circulatory and nervous manifestations but these are as a general rule of an evanescent nature. When X-ray fails McGuffin says radium usually succeeds and vice versa. The advantages of X-ray treatment are considerable. There are no fatalities with radiation; treatment is painless; it leaves no scar; the B.M.R. is reduced. It is suitable in cases of malignant recurrence. Crile (The Thyroid Gland. Crile and his Associates pp.263-265) records a severe case of cancer of the thyroid in which he had a very happy result by what he describes as decompression. He made a collar incision over the swelling and relieved the pressure by dividing the perithyroid muscles. Subsequently he closed the skin wound and applied X-ray treatment with most excellent results. On the other hand, Mayo records two cases of carcinoma (Med. Record June 18th 1921) due to X-ray treatment of the neck. A serious drawback to radiation is the length of time re-

quired to reduce the toxicity and complete the treatment. Again as the result of bad technique an unsightly X-ray burn may be produced. I have seen teleangiectasis follow a radium burn. Furthermore, if radiation fails and operation becomes necessary the surgeon has a much more difficult task before him owing to the perithyroid adhesions caused by the X-ray treatment. On the other hand Means and Aub (Archiv. Int. Med. 1919 XXIV 645-677) say that the chance of cure in exophthalmic goitre is as good with X-ray treatment as with surgery, and in fact radiation is preferable as the danger of a fatal issue is so much less with irradiation. Ludin (Centralle f.d. Greuz d. Med. Chir. 1915 XVIII 205-235) made a collection of 208 papers on X-ray treatment and in summing up the reports he said that usually with radiation there was a quick reduction in the pulse rate, that the tremor was reduced and nervous symptoms relieved and there occurred an almost immediate increase in body weight. One advantage of radiation is that in exophthalmic goitre the enlarged thymus may become

reduced. Berkman (St. Paul Med. Journ. 1916 XVIII pp.300-303) however, summing up the results at the Mayo clinic says that the results of radiation were good at the time but only gave temporary relief and remissions were common. C.H. Mayo (Surg. Gymaecol. and Obst. 1921 XXXII pp.209-213) says that generally X-ray treatment was a failure or only gave temporary benefit and unfortunately added to the difficulty of the subsequent operation. De Quervain says that as the result of radiation he has seen necrosis of the skin and underlying tissues down to the trachea (Goitre De Quervain p.200). There is however, great divergence of opinion as to the value of radiation. Florence A.. Stoney (Cure of Exophthalmic Goitre with Roenigm Rays Lancet 1916 pt.2.p.777) reports a series of 48 cases of Graves' disease. Of these seven gave up the treatment too soon to be worthy of consideration. Of the remainder 36 were so much benefited that they were able to return to ordinary life and work. She found it took about six months to cure a bad case but milder types were relieved in a much shorter period. It has to be observed

however that her treatment was not confined to radiation. She gave attention to the hygiene and diet. Oral sepsis was dealt with and when advisable she removed enlarged tonsils and adenoids. Tower and Crile (The Thyroid Gland pp. 223-250) say that whilst X-ray is a simple procedure right dosage can only be guessed at. If the dose is sufficient to kill the thyroid cells they say myxoedema may follow whilst if it is insufficient to effect this then a relapse may be expected. Delay in unsuccessful cases leads to serious secondary changes in the heart, liver and central nervous system.

Whilst there is divergence of opinion on the relative merits of operation and radiation it would appear that in certain cases radiation may be a useful adjunct to operation. Eugene Pool (Annals of Surgery Jan. 1927 New York pp.120-127) speaking of malignant growth of the thyroid says that cancer which is not limited by the capsule of an adenoma is rarely cured by surgery and consequently he advises, first, the removal of the adenoma and ,secondly, irradiation of the

field already operated on.

Radium may be said to be gaining ground in the therapy of hyperplastic goitre. G.W. Mowers (North West. Med. Seattle 1919 18.153) reports excellent results with this method of treatment. D.Turner (Edin. Med. Rev. 1919 22.79) has treated 50 cases with benefit in all but one woman who died within a fortnight of exposure. All the 50 cases were suffering from definite Graves' disease. Loucks (R.E. Loucks Amer. Journ. Roentology New York 1921 8.730) says radium is the treatment of choice but according to McCarrison (Thyroid Gland p.234) the whole subject of radiation in goitre is sub judice.

Electricity. Galvanism and the static current have been approved of by some. Bram considers galvanism applied once a week for 10 minutes over the thyroid swelling by means of a moistened sponge a satisfactory supplement to other forms of treatment. The static main current he gives daily or twice or thrice a week according to the case. He considers that if properly applied electricity is harmless and whilst in some patients no good may result, in others the period

of general treatment is considerably shortened.

Other methods.

Injection of boiling water into the goitre has been recommended by Porter (Journ. Amer. Med. Assoc. 1913 pt.2 p.61). His idea is to produce an aseptic necrosis with eventual reabsorption of necrosed elements. This method has been tried by Mayo and others. The result is a marked oedema and sometimes a fatal issue. Ochsrer employs phenol and boiling water. Watson (L.E. Watson New York Med. Journ. 1916 103. 791) has advocated injection of quinine and urea to relieve hyperthyroidism. There is no doubt that injection of boiling water is a dangerous procedure.

Injection of Iodine, 20-30 m. of a solution made up of 1 part iodine and 12 parts absolute alcohol was employed by Sir Felix Simon. Although a certain number of successful results were obtained the mortality was high. Dyspnoea and suffocation may follow the injection. Rose of Zurick (Der Kropftod und der Radicalkur des Kropfes Arch. f. Klin. chir. Vol. XXII) records six deaths on the operating table or very soon after. Seitz (Der Kropftod durch Stimmbundlah-

mung Langenbeck Archiv. f. klin. chir. XXIX I) tells of a female patient who after the injection of 10 minims tincture of iodine into her goitre felt first a numbness in her left arm, then she lost her speech and this was followed within twenty-four hours by convulsions and death. Dr. Krieg (Plötzlicker Tod.durch parenchymatose Injection von Jodtincteur unum fibrosen Kropf Mediz. Correspond. Bl.d. Wurtemb. aerztl Landesver, Stuttgard 1884 pp.145-149) injected two minims of the tincture of iodine into the neck of a fifteen year old female cretin and death followed in two minutes. Perchloride of iron has been used for injection in cystic goitre but the danger of haemorrhage, ,sepsis and adhesions is very considerable.

Serum therapy is another measure that has been used in hyperthyroidism. Serums were administered on the hypothesis that they are capable of neutralizing the excess of thyroid secretion in the blood and so overcoming the hyperactivity of the thyroid gland. Moebius used the serum of thyroidectomised sheep. This preparation he called thyroidin (Moebius O.

Schmidt's Jahob. 1886, 210). Lanz tried "rodagen", the dried milk of thyroidectomised goats (Lanz.O. Nederlands ch.Tidschr. v. Geneesk Amsterdam Feb.24th 1916). S.P. Becke (Interstate Med. Journ. St. Louis 1912 XIX 409-414) injected the nucleoproteid of the thyroid gland and also thyroglobulin into rabbits and used the cytolitic serum from these rabbits in 2000 cases. of hyperthyroidism. Beche (Monthly Cyclopoedia and Medical Bulletin New Series XVII No.3 1914) reports the treatment of 3000 cases with 50% cured or greatly improved and 30% to some extent benefited. According to Berry (Surgery of Thyroid Gland Brit. Med. Journ. 1913 pt.1.pp.583-591) the results are good in early cases but not in real typical cases of Graves disease.

Evacuation and drainage are methods only to be resorted to in cases of suppurative thyroiditis. Thyroiditis may arise by direct infection, by contiguity from a focus in the thyroid vicinity or by the blood stream as happens sometimes in Mumps, Influenza and Scarlet Fever (Lambert Rogers April 23rd 1927 Lancet pp.868-869). In the Lancet of Jan.29th, 1927 it was reported that at the Lahey clinic out of 3000

operations on the thyroid only three were for suppurative thyroiditis.

Tapping with trocar and canula has been tried in cystic goitre but it is altogether a questionable procedure.

Thyroid deficiency.

In a thesis on goitre it is necessary to make reference to the above condition. Apart from the occurrence of cachexia thyreopriva in the early days of thyroid surgery, even to-day deficiency is not unknown following surgical interference. On the other hand in endemic areas conditions of hypothyroidism are common. As the result of degenerative changes in an enlarged thyroid the healthy tissue may be so encroached upon that ultimately a condition of anatomical and functional deficiency may be found. In Graves' disease too, apart from excessive radiation, a change from hyperthyroidism to hypothyroidism may take place of a spontaneous nature. Goitrous mothers are also apt to give birth to hypothyroid children. In thyroid deficiency treatment is required whether that deficiency be partial or complete, whether it be congenital as in cretinism or acquired as in myxoedema or following

operative interference as in cachexia strumipriva. In surgical cases the deficiency may only be temporary and opotherapy required only till compensatory hypertrophy has time to take place. As regards cretinism early diagnosis is all-important. In order to do a cretin real good you have to catch him early, (R. Hutchison Dis. of Children. p.280), and if you do so and treat him properly he will grow up into a child who is practically indistinguishable from one healthy and normally developed. If treatment is not begun till the child is a few years old you are too late to render effectual help at least as regards mental development. Hutchison (Index of Treatment p.224) advises an initial dose of ½ to 1 grain of the dry thyroid in a powder or tablet each night. The dose should be gradually increased up to 5-7 grains daily. In myxoedema thyroid substance may be taken as a tablet or liquor thyroidii may be used. Some prefer the raw gland lightly fried on the outside or minced and taken with syrup. The liquid extract is said to be best but the tablet form is most convenient. The patient

is best in bed when treatment is begun. It has to be remembered that these patients do not tolerate the treatment as well as healthy individuals do. Regulate the dose by the body weight and the rate of the pulse. O. Leyton (Textbook of the Practice of Medicine F.N. Price 1926 p. 449) says in myxoedema the initial dose should be 1½ grains of the dried thyroid three times a day and if this dose does not produce any bad effects it should be gradually increased until palpitation, tremor, restlessness or sleeplessness is manifested. The dose should then be diminished slowly till the dose is reached at which these symptoms disappear. This dose is continued for life. The patient should be advised to lead the life of an invalid at least until the optimum dose of thyroid is reached. This will probably be about 5 grains daily (George R. Murray. Index of Treatment pp.665-666) It is well to stop the treatment for short periods from time to time. Intolerance, it should be remembered, is sometimes indicated by coryza (McCarrison Thyroid Gland 1917 p.193). Attempts have been made from time to time to graft thyroid tissue on the human subject. Bircher (Das Myxoedema und die

cretinische Degeneration. No.357 Chir. No.110.1888-1890. Volkm. Klein. Vort) was the first to transplant human thyroid tissue into the abdominal wall. In 1883 Kocher and Bircher demonstrated that transplanting was a good therapeutic measure. Heteroplasty, the implantation of animal thyroid into man, appears to be quite useless. Good results, however, have been obtained by homoplasty and autoplasty. Cristiani H. (Effets therapeutiques de la griffe thyroidienne chez l'homme. Congres internat. Lisbonne 1906) advocated the subcutaneous method of transplanting. This is called grafting "en semis". As many as twenty five to forty grafts, each the size of a rice grain, are placed below the skin. Voronoff and De Quervain place their grafts in the anatomical site of the thyroid gland. Kocher places the graft in the tibia. He insists that the graft must be the same size exactly as the hole made in the tibia. There must be no dead space between the graft and the bone. The graft must be placed in the tibia as soon as it is removed from the donor and it must not be more than twice the size of a cherry stone.

(Kocher Th. Die Schilddrusenplantation arch. f. klin. chir. t. 87. pt.1. 1908). The essentials of the operation are perfect haemostasis, strict asepsis, and immediate implantation of the graft. The myxoedematous condition of the patient is much against the success of the operation so it is wise to submit the patient to a period of intense opotherapy before attempting the operation.

Llewellyn Jones Llewellyn in the Prescriber of last year (Prescriber Nov. 1926 Vol. XX pp.403-408) referring to the correlation of thyroid deficiency with rheumatism in this country said that in rheumatic children we are faced with a basal hypothyroidism which entails a general suboxidation and he laid emphasis on food acidosis and fatigue acidosis in determining the onset of acute rheumatism. He suggested that in these cases thyroid substance should be combined with salicylates in treatment.

There is no doubt but that there are many obscure conditions which are associated with hypothyroidism that respond to thyroid substance more readily than to any other therapeutic agent.

The Operative Treatment of Goitre.

Extirpation of the thyroid gland typifies the supreme triumph of the surgeon's art. A familiar malady for thousands of years and frequently fatal, it was considered an inoperable affliction or dispensation of Providence causing suffocation, difficulty in swallowing, cardiac difficulty, and disfigurement (William S. Halsted. Baltimore. John Hopkins Hosp. Reports Vol.XIX 1920 pp.71-257). Mandt was the first to record a genuine extirpation of a goitre by Albucasis. This operation was done about 940 A.D. (Der Kropf Geschichtl. u. Extirpation dsselben, Rusts' Magazin f.d. gesammte Heilkunde, Berlin, 1832 Vol. 37 pp.390.412. 413). G.B. Gunther records the first 41 cutting operations performed for the removal in part or in totality of "struma lymphatica". (Operative Behandlung des Kropfes (Struma) Lehre v. d. blutigen operationen am Halses des menschlichen Körpers. Leipzig u. Heidelburg 1864 p.369). Foédére (Dictionnaire des sciences médicales Vol.XVIII p.555) says the operation on the thyroid has even been done by the "ignoramus", and intoxicated people have cut away large goitres

without disaster. Nevertheless Diffenback (Die Operation des Kropfes. Die Operation Chirurgice Leipzig 1848 Vol.II.pp. 331-340) in his day said "the operation for goitre is one of the most thankless and most perilous of undertakings, which, if not altogether prohibited, should at least be restricted to certain varieties of the malady." Gross also (System of Surgery 1864 Vol. 2 p.394) stated that "no honest and sensible surgeon would ever engage in it". Bruberger (Ueber die extirpation des Kropfes nebst einem geheilten Fall von Total Extirpation einer grossen mit breiter Bases aufsitzenden Struma hyperplastica und statistichen Bemerkungen D. Militärarztl Zeitschrift Berlin 1876 Jahrg. 5. p.447) gives the operative story from 1785 to 1876 and describes what appears to be the first recorded case of "status thyreopriva". Then in 1877 Adolf Suskind's thesis appeared (Ueber die Extirpation von Strumer Inaugural obhandlung. Tubingen). He deals with the treatment by operation from the end of the eighteenth century up to 1877. He gives Germany the place of honour. In France, he says, the operation was most emphatically condemned. In spite of this

there was a French surgeon of note, Pierre Joseph Desault, who held views contrary to most of his surgical confreres in France on the surgical treatment of goitre. He was probably the very first to dissect the firmly adherent gland from the trachea (Observation sur l'extirpation d'une partie considerable de la glande thyroide. Journ. de Chirurgie Paris 1792 t.iii p.3). In Italy probably the most renowned surgeon was Luigi Porta. He was the first known surgeon to ligature both superior and inferior thyroid arteries (Luigi Porta Della alterazioni pathologische delle arterie par la ligature e la torsione Milano 1845). In Great Britain Sir Wm. Blizard (reported by Burns. Observations on the Surgical Anatomy of the Head and Neck. Edinburgh 1811 p.202.) was the first to ligate a thyroid artery with a view to the cure of goitre.

In this country Green is usually credited with the first excision of a goitre. Holmes operated on a cyst weighing seven pounds which hung down below the patient's waist. Heron Watson (Edin. Med. Journ. 1874 Vol.XIX p.252) however, was the dominant figure in Britain in regard to thyroid sur-

gery. In the United States the most prominent surgeons on the thyroid were Nathan Smith, Cooper, Green, and Maury. In Germany Hedenus of Dresden in 1800, in spite of men like Richter (who said he never had performed this operation, and never would) completed in a fairly bloodless manner and without an anaesthetic an operation on a thyroid gland of considerable magnitude. It was really a feat of which Halstead speaks highly in contrast to his description of Klein's "detestable performances". Von Bruns and Theo Billroth were two of Germany's ablest operators. They did some excellent work. The significance of Billroth's work is reflected in the writings of his school. It was here that von Mickuliez, Wölfler, von Eiselsberg and many others gained their experience. The next surgeon to mention is probably the most notable figure among thyroid surgeons. When only thirty-one years Theodore Kocher succeeded Lucke at Berne. To give any adequate expression of his work would be difficult. More advance was made in thyroid surgery from 1873 to 1883 than in all previous years or in fact in all the years subsequent to that period. This, however, was made possible by the work of

Lister in this country. In 1883 Kocher published his famous paper - Ueber Kropfextirpation und ihre Folgen Arch. f. klin. chir. /t. 29 p.593, 1883 - in which he considered the evil consequences of total strumectomy. He standardised the operation of thyroid lobectomy. He died in 1917 having performed about 5000 operations on the thyroid gland. John D. Pemberton (Present Day Surgical Treatment of Diseases of the Thyroid Gland Journ. Amer. Med. Assoc. 1925 LXXXV 1882-1886) after a reference to the adverse criticism of thyroid operations by Gross goes on to show how different the position is to-day with a hazard that may be put at less than 0.5%, thanks to the work of men like Billroth, Kocher, Mikuliez, Halstead, Mayo and Crile who have developed and standardised the operative technique to a high pitch of perfection. "Thanks to the efforts of Billroth and Kocher and to the influence of the antiseptic treatment of wounds", said Mikulicz "the technique of strumectomy has in a short time been so highly perfected that one soon will not hesitate to perform solely for cosmetic reasons an operation which Diffenbach shuddered to contemplate".

The field of thyroid surgery is chiefly limited to the different forms of hyperthyroidism but operation is sometimes demanded in simple goitre on account of pressure symptoms. Most surgeons are agreed that large adenomata should be removed by operation. Toxic symptoms as a rule take years to appear. In the early stages of toxic goitre operation gives an excellent prognosis but if operation is delayed till the myocardium has undergone pathological changes from prolonged toxaemia the outlook is much more serious. As Parsons says (Annals of Surgery Jan. 1927 pp.107-115) in adenoma of the thyroid gland "operation is the best treatment for all adenomata and early operation is essential". A rapidly growing adenoma should always give a suspicion of malignant disease. If the suspicion is correct the only hope of saving the patient's life is an early operation before the cancer penetrates the capsule and affects the surrounding tissues. Sometimes these adenomata are of an enormous size. Robert B. Drury of Columbus figures one (Ohio State Med. Journ. March 1927 pp.227-228) of considerable dimensions hanging over the left breast and consisting of large multiple adenomata.

Whilst there is general agreement about operation in adenomata the same cannot be said with regard to the goitre of Graves' disease. The American physicians are convinced that the rationale of surgery is entirely wrong, that not only does surgery not cure the patient but – if it be true as Crile says, that the thyroid makes life worth living – the removal of the thyroid leaves the patient in a very serious state. Doubtless the surgeon is not altogether to blame. The dormant attitude of medical men in general has much to do with the present state of affairs. Even Llewellyn Barker (New York Med. Journ March 2nd, 1921 p.355) confessed that even after operation sufferers from Graves' disease rarely regained perfect health and required close medical supervision for a long time, sometimes for the whole of their lives. This shows that operation may not cure the patient, after he has run the operative hazard. It is admitted that the operative hazard is not nearly so serious as it was previous to the use of iodine as a preoperative measure. To-day in hyperthyroid cases before any surgical treatment is

given a course of iodine is undertaken. Plummer says (Collected Papers of the Mayo Clinic 1925 pp.473-489) that the use of Lugol's solution prior to operation has reduced the surgical mortality from 3.5% to 1%.

As a preliminary measure ligature of the thyroid arteries is advocated by many surgeons. In 1814 Walther tied both superior thyroid arteries (Neue Heilart des Kropfes durch die Unterbindung der oberen Schlagadaren Salzbuch 1817 p.25). Gunther collected 21 cases of ligature of the superior thyroid arteries resulting in the complete cure of two cases, the improvement of fourteen and the death of three patients. Wolfler advised the ligature of both the superior and inferior vessels. Berry (The Thyroid Gland p.242) considers ligature of the inferior thyroid artery a difficult operation whether done by Velpean's method, or that suggested by Langenback. Kocher favoured tying three out of the four vessels. Simultaneous ligature of the four arteries Berry considers quite as severe an operation as partial thyroidectomy (J. Berry Brit. Med. Journ. 1913 pt.1.pp.583-591). Ligature of the arteries may be performed as a preliminary

test to see what reaction is made. It may be done prior to operation to limit haemorrhage at the subsequent operation, However ligature of the vessels is done sometimes in the hope of producing atrophy in the gland. It is still the method of choice for vascular goitres of moderate size and especially is it considered suitable in some cases of exophthalmic goitre. All four vessels may be tied in vascular goitre without fear provided that the connection between the gland and the surrounding tissues has not been disturbed. Generally, however, it is enough to ligature the two inferior arteries, one of the superior vessels and part of the remaining superior artery. Atrophy does result but it seems that after a time a return to the original condition takes place. In simple non-vascular goitre ligature as the sole method of treatment ought to be abandoned but in Graves' disease ligature of the arteries not only causes a diminution in the size of the goitre but causes in many cases a more or less definite disappearance of the symptoms.

Operation Cases. Whilst it is true as Fahrini says (Surgical Treatment of Goitre Canad. Med. Assoc. Journ. Oct. 1926

pp.1184-1194) that the field of surgery is largely limited to the different forms of hyperthyroidism operative procedure is sometimes necessary on account of urgent dyspnoea. Apart from dyspnoea operative interference is seldom advisable in the goitre of early life. Apart from dyspnoea operation is the best treatment in large cystic thyroids. Again the presence of large nodules in a goitre should suggest operation before toxic symptoms have time to work havoc in the patient's organs. Operation is also called for in toxic adenoma and malignant disease.

Pre-Operative Care.

Except in urgent cases careful preparation should be made prior to operation. No operation on the thyroid gland is desirable where the patient has recently suffered from tonsillitis. A period of rest should be enforced prior to operation.

Drugs. The patient on arrival at the hospital is put to bed. Lugol's solution is given in 10 minim doses three times a day. Other treatment may be required such as digitalis,

strophanthus, or perhaps quinaidine. In hyperthyroidism Loeper and Ollivier found borax helpful (Bull Soc. Med. d'hop. Paris 1925 49.734-737). In cases of sleeplessness it may be necessary to administer veronal. Restlessness is combated by an ice cap to the heart.

Diet is liberal but vegetarian. Crile urges that plenty of fluid be given. He advises 3000-7000 ccs. of fluid per day. Quinine urea may be tried as a preliminary step to test the reaction. If there is no reaction then ligature of the superior arteries may now be safely undertaken. The day before operation a purgative is given. The field of operation is carefully prepared. It is first shaved clean, then scrubbed up with soap and water. All the grease is removed. A one in thirty carbolic acid dressing is now applied.

Anaesthetic.

Different operators have different ideas about the anaesthetic. If general anaesthesia is decided upon - and this is practically essential in children - the anaesthesia should be light. Crile's method of stealing the gland does not appear to have found favour with many surgeons. Crile

believes his method prevents "stage fright". He gives analgesic doses of nitrous oxide and novocain for local application (B. Synder Thyroid Gland Crile etc. pp.205-210). De Quervain uses a 0.5% solution of novocain with the addition of adrenalin. Local anaesthesia alone has this advantage that vomiting is less likely to occur after the operation. There is also less likelihood of bronchitis and the function of the recurrent laryngeal nerve can be tested in a conscious patient during the operation. The local anaesthesia may be maintained by subcutaneous and subfascial injection alone or the nerve trunks or cervical roots may be injected as well. The patient should be strapped to the table. The field of operation should be protected by a "Kocher screen". Some differences of opinion exist among surgeons as to the best skin incision to make. All agree that it should be a very free one. Erichsen advises an incision in the middle line of the neck. Kocher prefers a transverse curved incision following the folds of the skin, the "incision en cravate" as it is called and this is the one generally adopted. Berry advocates an oblique incision parallel to

the inner margin of the sterno-mastoid muscle. The succeeding steps will depend on the operation decided on. An operation first practised by Jabonlay is called "exothyropexy". In this operation the operator cuts down quickly on the thyroid and having exposed it well he dislocates it through the wound and leaves it exposed to the air, the object being to relieve tracheal pressure and at the same time induce atrophy. It has the advantage of being a quick operation and one not requiring great skill but the danger of haemorrhage and sepsis condemns it altogether.

Division or Resection of the Isthmus is another operation first employed for the relief of urgent dyspnoea. Temporary relief usually follows this comparatively simple operation but with the healing of the wound the difficulty in breathing usually recurs. (Fred. Page Green's Encyclop. pt.23 p.21). As a matter of fact the operation is based on a false foundation for the dyspnoea as a rule is due to lateral pressure and flattening and not antero-posterior closure. Any relief that is obtained by this operation is the result of the general shrinkage of the gland following the escape of col-

loid from the cut surfaces.

Total extirpation of the thyroid gland is never attempted now except in malignant disease. To-day all thyroid operations aim only at a partial removal of the gland. Hemi-thyroidectomy consists in the removal of one of the lobes, usually the more obtrusive one. Although a comparatively easy operation it leads to lateral displacement of the trachea, involves the destruction of the two parathyroids on one side and there is great danger of injuring the recurrent nerve.

Resection. Mikuliez of Cracow gave this name to an operation particularly suitable for parenchymatous goitre. (Ueber die Resection des Kropfes nebst Bermerkungen ueber die Folyez-ustande der Total exstirpation des Schilddrüse Centralblatt. f.chir. Dec. 19th 1885). He separated the right lobe from its surrounding tissues by means of blunt forceps, tying the vessels as they appeared. Then he placed double ligatures on the superior thyroid artery and vein of the right side and cut through between his ligatures. Snipping round with his scissors he freed the bulk of the lobe from the tissue in front and to the side of the trachea. The pedicle was then

separated into several parts with blunt scissors and each part was firmly ligatured. Then the lobe was removed and the wound closed in the usual way.

Enucleation means the peeling off or the decortication of one or several intraglandular nodules. (Crotti Thyroid and Thymus p.512). This is the usual operation for adenoma. It is also the operation for cystic goitre. It was performed in 1840 by Luigi Porta (Delle malattie e delle operazioni della ghiandola tiroidea). Whether solid or cystic these tumours are usually encapsulated. The surgeon after exposing the gland cuts down through the thyroid tissue till he reaches the capsule, tying vessels as he proceeds. The fore-finger is now imployed to go round the adenomatous mass and free it from the thyroid tissue in which it is embedded. The nodule is thus removed and after the cavity is dried out sutures are drawn through its walls closing up this space completely.

Resection-enucleation. Many goitres are partly diffuse and partly nodular. This led Kocher to invent a combined operation which is partly enucleation and partly resection. This

he termed resection-enucleation (Correspondenz blatt f. schweiz Aerzte, Basle, 1889 p.38). After the "incision en cravate" the platysma is divided and the anterior jugular veins are tied. The inferior thyroid artery on one side is not ligatured. De Quervain makes ligature of the inferior thyroid vessel a constant practice in lobectomy. The thyroid space is now entered, the upper pole of the lobe is reached, and securely ligatured. The entire lobe is now freed from its connections except on its posterior surface. The avoidance of the posterior surface is of primary importance. The lobe is now delivered either by means of a loop of stout thread passed several times through the lobe or by a Kocher scoop or better still with the index finger. A melon slice section is now made and any large nodules that are present are freed by the index finger and removed with the slice. The remaining part of the lobe is now reconstructed by a continuous suture. The prethyroid muscles are reunited, the platysma stitched and the skin sutured. A drainage tube is inserted for 24 hours.

It is important in these operations to decide correctly

how much gland tissue can be removed without causing hypothyroidism. If the tissue is healthy it is generally held that if not more than three quarters of the gland is removed no hypothyroid effects will be produced. If, however, the tissue is not healthy it is necessary to be more conservative in our operation leaving considerably more tissue behind. Some operators, such as Crile, advise packing the wound with two gauze strips before inserting the rubber drain.

In operations on substernal goitre the anaesthesia and general technique are similar to the above. As a rule the mass can usually be elevated from the thorax without difficulty. The finger may be used to enucleate. The cavity is then packed with gauze. In some cases cutting the sternal end of the sterno-mastoid muscle may facilitate the enucleation.

Halsted's Operation.

A collar incision is made accurately in a wrinkle of the neck. The platysma is divided and dissected up with the skin flap care being taken to avoid the veins. The lower flap is dissected in the middle line to expose the

manubrial notch. The sterno-hyoid and omo-hyoid muscles are now gently raised from the sterno-hyoid muscle and retracted outwards, all veins of any consequence being ligatured. The sterno thyroid is now split with a blunt instrument and retracted outwards to expose the superior thyroid vessels. The superior pole can now be hooked forwards by the index finger. Two clamps are applied near the tip of the gland and a cut is now made between the clamps. The lobe is now gradually divided towards the trachea. When this is accomplished the lobe is rolled inwards, the loose extrinsic capsule is divided and gently sponged backwards with the "Breslan roll" of tightly wound gauze. The vessels are now clamped well away from the recurrent nerve and the parathyroid glands. (Halsted does not advocate tying the trunks of the inferior thyroid vessels). After this the lobe is rolled outwards and the isthmus is freed from the trachea by a long narrow blunt dissector. After tying bleeding vessels the isthmus is divided. The lobe is now resected from within outwards. Cut vessels are clamped. Then the stump is stitched up with fine silk. The little stump of the superior pole is then

drawn down and transfixed with silk. The wound is closed without drainage.

After the operation the patient is put back to bed in the semi-recumbent position. For the first few days only liquid food is allowed. The patient is encouraged to drink large quantities of fluid as this helps to ward off acidosis. A hypodermic injection of morphia is given to induce sleep and discourage coughing. If a drainage tube has been inserted it ought to be removed at the end of 24 hours. If all is well the sutures are taken out on the third day and the patient is allowed up on the fourth or fifth day, but if the operation is for Graves' disease rest is much more prolonged.

One of the most dangerous post operative complications is haemorrhage. This may be the result of the slipping of a ligature. Suffocation may ensue from clot pressure on the trachea if the wound is not rapidly opened and the clot removed. Light packing afterwards with gauze soaked in haemostatic serum may be helpful in these circumstances.

Loss of voice is another troublesome condition that

sometimes occurs. Statistics show from 4 to 14% of instances of actual injury to the recurrent nerve. The nerve runs the greatest danger in the classical operation of hemithyroidectomy as in this operation the nerve is apt to be included in ligaturing the lower pole. Loss of voice may however be the result of too much dragging of the nerve when dislodging the goitre. If there is paralysis or paresis of the posterior crico arytenoids the change in phonation may be slight but it will be found that the patient is unable to give a clear dry cough. In the bilateral operation it is a good rule to test the voice after resection of one side before proceeding to the resection of the remaining lobe. The ability to test the voice during the operation is one of the advantages of avoiding general anaesthesia. Care to leave plenty of thyroid tissue at the base, the avoidance of rough manipulation and precision in the application of ligatures are the best prophylactic measures for the safeguarding of the nerves and parathyroids against subsequent tetany, loss of voice and pneumonia.

There is sometimes considerable shock after thyroidectomy. It is in these circumstances that transfusion may prove very helpful. As Sample says (The Thyroid Gland, Crile and Assoc. pp.267-269) "it is the most successful single therapeutic agent at our command". If sufficient preoperative care has been taken and the patient has received plenty of fluid acidosis is not likely to occur.

Prognosis:- Crile (Ibid. pp.283-292) reported 1783 thyroidectomies with a mortality of 1.4%. In Switzerland from 1911 to 1915 the fatality rate for 7809 thyroid operations was 0.66%. The most frequent cause of death in those Swiss goitres was found to be pneumonia. This indicates the danger of operating on elderly patients with bronchial trouble. Other causes of death were wound infection, haemorrhage, pulmonary embolism and tetany. In childhood it is not often that operation is required. When it is required in these young people it is usually on account of acute dyspnoea. In most surgical goitres it is true that there once was a time in their history when they were non-surgical and curable without operation. In young persons adenomatous

tissue is seldom found in the thyroid, the swelling is diffuse and fairly soft and altogether very different from the large degenerated, cystic, nodular, fibrosed and calcified gland of goitrous patients past middle age. Again Graves' disease is not a local thyroid disease but a general neuro-endocrine dysfunction in which the thyroid enlargement is no more the main factor in the clinical picture than is splenic hypertrophy the main or only factor in enteric fever. If exophthalmic goitre received due attention from the physician and if simple goitre was treated in its early stages the number of cases that come for operation would be very considerably reduced. It is true as McCarrison says in his review of Dr. J. Eason's recent book on Exophthalmic Goitre that "the measure of our independence of thyroidectomy in Graves' disease is a fair measure of our advance in knowledge". (R.McCarrison. B.M.J. May 1927 p.963).

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SECTION 7.

S U M M A R Y.

A. Gland Function and Dysfunction.

Two distinct phases of physiological activity have to be recognised. One is the passive phase of vesiculation, whereby the excess or reserve of colloid is stored within the epithelial column. The other phase is that of active secretion in which a substance different in nature from the colloid is elaborated by the activity of the thyroid gland. Two types of endemic goitre have been described (1) a chronic hypertrophic type in which secretory activity is marked and (2) a chronic vesicular form in which colloid storage predominates.

Thyroxin isolated by Kendall and synthetised by Harington is at least one of the active hormones of the thyroid gland. There seems to be a multiplicity of function in the thyroid gland. At least four different functions are known.

Graves' disease is not a local thyroid disease but a

general neuro-endocrine dysfunction. Operation often fails to cure exophthalmic goitre. As McCarrison says "the measure of our independence of thyroidectomy in Graves' disease is a measure of our advance in the knowledge of the proper treatment".

The thyroid, thymus, and parathyroid glands appear to act in combination. The thyroid is the main organ; the parathyroids act as sentinels to thyroid efficiency; the thymus is the reserve for fat or lymphocytes.

Paton and his co-workers have shown the importance of the parathyroid glands in the metabolism of guanidin and the control of muscle tone. They also believe that the parathyroid glands are implicated in idiopathic tetany.

B. Distribution.

Goitre extends over almost the whole of the inhabited earth. It is not peculiar to any particular geological formation.

In England hills seem to play a part in distribution. In the north of England goitre is associated with the Pennine

range. On the east side, the goitre incidence in children is low above the River Tyne, but gradually increases as Bradford and Leeds are approached. In children the incidence is higher on the west than on the east. In Manchester and Preston the incidence in school children is specially high.

Stiner found that the incidence of goitre in school children in Switzerland bore no relationship to the prevalence amongst adults. In England Berry drew attention to the correlation between the distribution of goitre amongst adults and the occurrence of calcareous limestone and sandstone. The highest endemic centres in this country among children are also associated with limestone and sandstone.

In England goitre among school children is associated with the Pennine, Cotswold, and Mendip ranges. This agrees with the distribution of cardiac rheumatism. The incidence of both cardiac rheumatism and simple goitre is specially high in Lancashire. It has been said that cretinism is most prevalent where the incidence of goitre is high (McCarrison). According to Hercus this is not true for New Zealand. In

Manchester there is a considerable incidence of goitre but cretinism is relatively rare. (S.M.O. report for Manchester for 1926). Two types of cretinism have been described. The so-called myxoedematous type is well known and is characterised by perpetual infancy of body and mind in well defined cases. The other type of cretinism, nervous cretinism, as McCarrison calls it, is a kind of idiocy associated not with the ordinary stigmata of the cretin, but with cerebral spastic diplegia and tetany. This latter type occurs widely in India and Brazil but it is not unknown in this country.

Achondroplasia is not infrequent in goitrous areas. Hertoghe believed it to be due to thyroid dysfunction. Virchow and Eherth considered achondroplasia to be a form of foetal cretinism. There is a general resemblance between the two conditions but clinically achondroplasia has quite distinct features of its own.

C. Soil, Iodine and other Factors.

Whatever the causation of simple goitre may be it is undoubtedly contingent upon some disturbance in the iodine

supply.

A very definite relationship between the incidence of goitre and the amount of iodine in the soil has been established for New Zealand (Hercus, Benson and Carter) and parts of Switzerland (v. Fellenberg).

A new type of goitre, not associated with iodine deficiency has been described (McCarrison). The absence of green vegetables and fruit in a diet containing over 60% white flour and less than 20% protein seems important in the production of this form of goitre. The dominant feature in this type of goitre is insufficiency of vitamin B.

The soil iodine is clearly an important factor in the etiology. It is clear that the amount of iodine in the soil will determine the amount of iodine in the vegetable produce in any particular district. The quantity of iodine in the vegetables, plants, grass etc. will affect the iodine content in the dairy produce. This, however, only applies to those districts where the inhabitants live on their own produce. It is not applicable to a large town such as Manchester. The markets in this place are supplied

from a wide area outside the town. The soil iodine in Manchester therefore should not affect the goitre incidence here. As a matter of fact the goitre incidence is highest on the clay, in which the iodine content is high, and lowest in the glacial sand, in which the iodine content is low. The goitre incidence is high in Hulme and Clayton and low in Moston. The social conditions are good in Moston but this cannot be said of the districts in which the incidence is high. It seems true that goitre like rheumatism is more prevalent among the poorer classes. That the incidence is low among the Jews is clearly due to the wise dietetic habits that prevail amongst them. The care, too, that is taken of the pregnant Jewess is not without significance. Heredity and diet are clearly two important factors in the etiology of simple goitre. The goitrous mother is liable to have goitrous or cretinous offspring. I have found as many as six members of one family affected with goitre.

Berry, noting the great denudation in the highlands of Scotland and the low incidence of goitre in that region and

and also observing the prevalence of goitre in the north of England and the relatively abundant vegetation and calcareous limestone in that part, concluded that the cause of goitre was at least associated with the presence of minute inorganic particles in the water supply. This has not been proved.

Whilst goitre is theoretically due to iodine deficiency it is due in practice to a combination of factors. Intestinal toxaemia, fatigue, focal infection, and lack of balance in the diet have all etiological significance.

McCarrison's infective theory has not yet been proved. Rosenor's diplobacillus has not been definitely shown to be specific in goitre.

The importance of a fat-thyroid-iodine balance in the diet has been shown by McCarrison in his experiments on pigeons. The effect of feeding pigeons with faecal contaminated food has also been shown to be the production of goitre. McCarrison's conclusions however, with regard to the causation of goitre in the Gilgit fan have been keenly criticised by

Hercus and his colleagues. The New Zealand workers suggest that in this part of India where goitre is endemic deficiency of iodine is the probable cause.

D. Treatment.

Diet is one of the most important factors for consideration in the treatment of endemic goitre, sporadic goitre, and Graves' disease. For prophylaxis there seems no serious objection to iodised salt provided that care is taken to limit the iodine percentage to that suggested by the Swiss goitre commission. For school children iodostarin is probably best for preventive purposes.

In the treatment of endemic goitre iodine is the most effective drug. In sporadic goitre the best results are obtained with thyroid substance. Thyroid substance is the treatment par excellence for cretinism and myxoedema. To obtain results in cretinism early treatment is essential.

Iodine in weekly doses of 10 mgms. is quite safe for school children.

Intestinal disinfection with manganese, kaolin, thymol, sour milk, and naphtho benzol do not give striking re-

sults.

Electricity, X-rays, and radium in the treatment of goitre are still sub judice. X-rays seem to be helpful in some cases of exophthalmic goitre but surgeons complain that X-ray treatment makes a subsequent operation much more difficult.

Injection with boiling water or iodine is bad treatment; serum therapy is useless; tapping is risky.

Grafting for cretinism and myxoedema is very uncertain. Thyroid substance is the only remedy that is really effective. In cretinism treatment will be ineffective probably, at least as regards mental development, if not begun till the child is a few years old. The effect of thyroid medication in cases of spastic diplegia associated with tetany is important in diagnosis and prognosis.

Operation for simple goitre in children should only be done in cases of urgent dyspnoea.

If simple goitre received early and efficient treatment during school life (when many cases first occur) a large percentage would be cured. Adenoma is rare in child-

hood. In most surgical goitres it is true that there once was a time in their history when they were non-surgical and curable without operation.

In adenoma of the thyroid gland the only right treatment is operation and the earlier this is done the better except in very young patients.

Operation is also demanded in malignant disease of the thyroid. A rapidly increasing thyroid swelling should, as a rule, indicate early operation. Cure can only be expected in early cases.

Cystic goitre is amenable only to operative treatment. Exophthalmic goitre is not necessarily the portion of the surgeon. If this disease received adequate attention from the physician the number of cases of Graves' disease subjected to thyroidectomy would be greatly reduced. Thyroid enlargement is no more the main factor in the clinical picture of this disease than is splenic hypertrophy the main or only factor in enteric fever.

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CONCLUSIONS.

I have come to the conclusion

1. That goitre is a disease of almost universal distribution occurring in endemic, sporadic, and epidemic forms and is in this country largely associated with calcareous rocks.
2. That the function of the thyroid gland is to produce a secretion of a complex constitution of which thyroxin is an essential part.
3. That cretinism is a chronic disease arising through deficiency or absence of thyroid secretion and occurring in two distinct forms.
4. That iodine deficiency is one important factor in the production of goitre.
5. That toxic infection also plays an important rôle in the etiology of some types of goitre.
6. That the Jews owing to their characteristic dietetic habits enjoy great freedom from simple goitre.
7. That iodine is our sheet anchor both for prevention

and cure of endemic goitre and in weekly doses of 10 milligrammes is a safe and effective remedy where the thyroid enlargement is not of long standing.

8. That thyroid substance is effective in the treatment of sporadic goitre, and myxoedema, and in cretinism has a curative effect if commenced at an early age.

9. That operation is the only correct treatment for adenoma of the thyroid - and is demanded also in cystic and malignant disease of the thyroid gland.

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